New Catalytic Processes Based on Cyclizations of Allylstannanes with Late Transition Metals

MEMORIA que para optar al grado de

DOCTORA EN QUÍMICA

Presenta

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Madrid, octubre 2007

A mis padres y hermanas

A Alejandro

El trabajo recogido en esta memoria ha sido realizado en el Departamento de Química Orgánica de la Universidad Autónoma de Madrid y en el Institut Català d'Investigació Química (ICIQ), bajo la dirección del Profesor Antonio M. Echavarren, a quien agradezco la formación que he recibido, el haberme permitido trabajar con independencia y el transmitirme su inagotable afán de ir cada día un poco más lejos. Este trabajo se ha llevado a cabo gracias a una beca predoctoral de Formación de Profesorado Universitario de la Universidad Autónoma de Madrid desde abril de 2003.

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Hasta el momento de redactar esta memoria, los resultados aquí descritos han dado lugar a la siguiente publicación:

"Intramolecular carbostannylation of alkynes catalyzed by silver(I) species."

Porcel, S.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2672-2676.

Contents

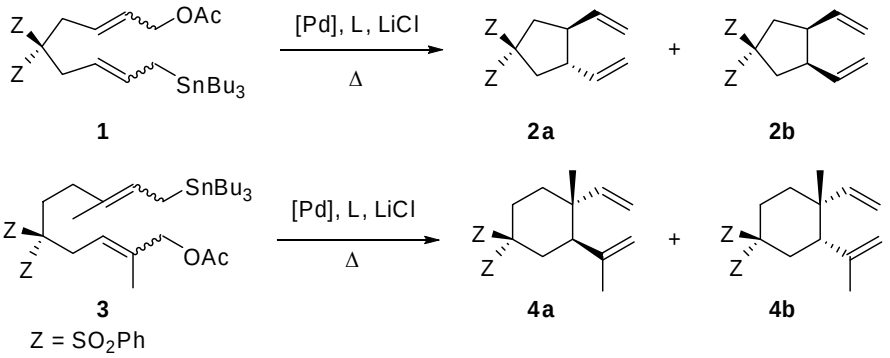
Esta memoria del trabajo de la Tesis Doctoral se ha dividido en dos capítulos. Ambos constan de una introducción general, en la que se han incluido los resultados previos del grupo, para poner en contexto el trabajo de investigación realizado, y de un apartado de discusión y resultados en el que se ha abordado el estudio de reacciones de ciclación de alilestannanos.

En la introducción del primer capítulo se recoge una revisión general de reactividad de complejos de alilmetal, poniendo mayor énfasis en aquellas reacciones más relacionadas con el trabajo de investigación desarrollado. En el apartado de "resultados y discusión" de este capítulo, se exponen los resultados obtenidos en el estudio de la reacción de acoplamiento intramolecular de alilestannanos-alilacetatos catalizada por Pd(0), Rh(I) y Au(I). La introducción del segundo capítulo contiene una revisión de reacciones de catálisis homogénea con plata y de reacciones de carboestannilación de alquinos. De nuevo se han descrito aquellas reacciones que están más relacionadas con el trabajo de investigación desarrollado. Así, se han omitido las reacciones de cicloadición o de transferencia de carbeno y nitreno catalizadas por plata, que aunque recientemente están teniendo mayor desarrollo, no guardan relación con el tema de investigación desarrollado. El apartado de "resultados y discusión" del segundo capítulo se basa fundamentalmente en la publicación "Intramolecular carbostannylation of alkynes catalyzed by silver(I) species" (Porcel, S.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2007**, *46*, 2672-2676) junto con algunos resultados adicionales no incluidos en este trabajo.

Resumen

Capítulo 1.

El desarrollo de nuevos métodos de ciclación que permitan a partir de sustratos acíclicos sencillos la obtención de compuestos de una mayor complejidad estructural, constituye una de las áreas más activas de la química organometálica de los metales de transición. En este contexto, nuestro grupo de investigación había desarrollado un nuevo método de obtención de carbociclos de 5 o 6 miembros basado en el acoplamiento intramolecular de alilestannanos con alilacetatos catalizado por Pd(0) (Esquema 1).[1,2]



Esquema 1

A través de un estudio teórico del mecanismo de la reacción[1] se encontró que el acoplamiento alilo/alilo transcurría mediante un nuevo tipo eliminación reductora en la cual se formaba el enlace carbono-carbono a través de los extremos C3-C3' de los sitemas alílicos, y que dicha eliminación reductora tenía lugar sobre un complejo de dialilpaladio con dos ligandos L dadores o un ligando bidentado L_2. A pesar de que los aspectos generales del mecanismo de la ciclación se comprendían razonablemente bien, la estereoquímica del proceso no era fácil de justificar. Así, sorprendentemente, mientras la ciclación de **1** conducía selectivamente a los derivados con configuración *trans* **2a**, la ciclación de **3** daba lugar a los derivados **4b** con configuración *cis*.

Los carbociclos de 6 miembros con configuración *trans* son de particular importancia, pues son precursores de lobanos como el fuscol y el lobatrieno, diterpenos de origen marino con potente actividad inhibidora de la biosíntesis de leucotrienos.[3] Por

1 Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 3620-3628.

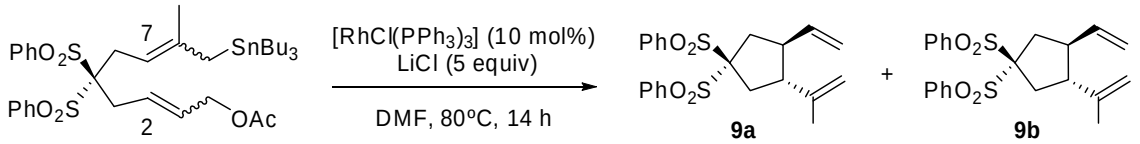
2 Revisión: Méndez, M.; Echavarren, A. M. *Eur. J. Org. Chem*. **2002**, 15-28.

3 (a) Gopichand, Y.; Schmitz, F. J. *Tetrahedron Lett*. **1978**, *19*, 3641-3644. (b) Shin, J.; Fenical, W. *J. Org. Chem*. **1991**, *56*, 3153-3158. (c) Chai, M.-C.; Wang, S.-K.; Dai, C.-F.; Duh, C.-Y. *J. Nat. Prod*. **2000**, *63*, 843-844, y referencias citadas.

esta razón como primer objetivo de este trabajo de Tesis Doctoral se propuso profundizar en el estudio de la esteroselectividad en la ciclación de derivados de tipo **3** con el propósito de invertir la preferencia observada en la ciclación.

Puesto que el mencionado estudio teórico indicaba que en la etapa de cierre del ciclo había involucrados dos ligandos fosfina, se comenzó analizando qué efecto tenía sobre la estereoselectividad de la reacción el empleo de fosfinas con características estéricas y/o electrónicas distintas. No obstante, en este estudio no se consiguió mejorar los resultados obtenidos con el ligando dppf (1,1'-bis(difenilfosfino)ferroceno) que anteriormente había dado una diastereoselectividad **4a**/**4b** de 1/3.[1]

Paralelamente a la búsqueda de condiciones para la obtención de carbociclos de 6 miembros con disposición *trans*-1,2-dialquenil de los sutituyentes, se encontró que los sustratos de tipo **1** dan la reacción de ciclación con el complejo $[RhCl(PPh_3)_3]$, bajo condiciones similares a las empleadas en la catálisis con Pd(0) (Esquema 2).

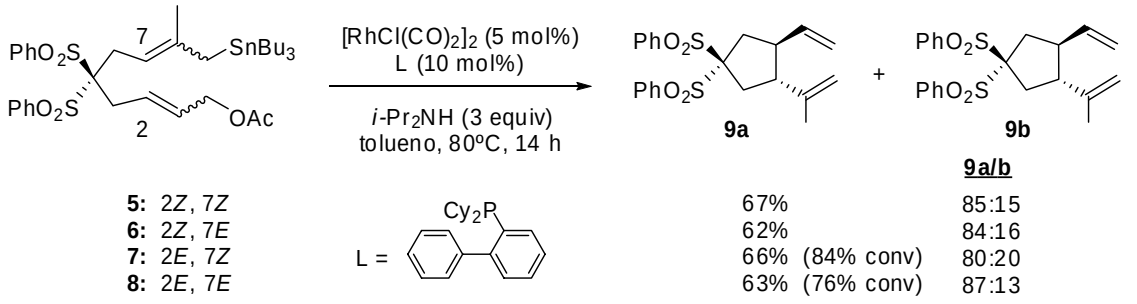


		9a/b
5: 2*Z*, 7*Z*	73%	87:13
6: 2*Z*, 7*E*	62%	81:19
7: 2*E*, 7*Z*	55% (88% conv)	54:42
8: 2*E*, 7*E*	73% (84% conv)	73:27

Esquema 2

Al igual que ocurre con los carbociclos de 5 miembros con Pd(0), la reacción catalizada por Rh(I) da mayoritariamente el isómero *trans.* No obstante, a diferencia de lo que sucede con Pd, los rendimientos dependen de la configuración del sustrato de partida; sustratos con una configuración *E* en el alilacetato dan rendimientos más bajos, y además la conversión no es completa. A pesar de que la estereoquímica del proceso es la misma que la observada con Pd, estos resultados eran de interés ya que esta reacción de acoplamiento intramolecular catalizada por Rh(I) no tiene precedente.

Además de $[RhCl(PPh_3)_3]$, se encontró que el dímero $[RhCl(CO)_2]_2$ también da la reacción de ciclación con rendimientos similares a los de $[RhCl(PPh_3)_3]$, bajo las condiciones indicadas en el Esquema 3.

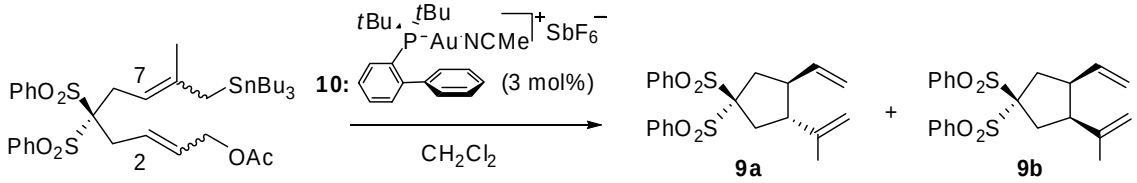


			9a/b
5: 2*Z*, 7*Z*		67%	85:15
6: 2*Z*, 7*E*		62%	84:16
7: 2*E*, 7*Z*		66% (84% conv)	80:20
8: 2*E*, 7*E*		63% (76% conv)	87:13

Esquema 3

Sin embargo, todos los intentos de ciclación del sustrato **3** precursor del esqueleto de seis miembros de lobanos y lobatrienos, empleando catalizadores de Rh(I), resultaron infructuosos.

Sorprendentemente, complejos de Au(I) resultaron ser los catalizadores más activos para esta reacción de ciclación. La reacción catalizada por Au(I) es estrictamente dependiente de la configuración del sustrato de partida y al igual que sucede con los complejos de Rh(I), los sustratos con una configuración *E* en el alilacetato reaccionan más lentamente y requieren condiciones más enérgicas (Esquema 4).



			9a/b
5: 2*Z*, 7*Z*	50ºC, 15 min	95%	100:0
6: 2*Z*, 7*E*	50ºC, 1h 20 min	92%	100:0
7: 2*E*, 7*Z*	80ºC, 19 h	47%	56:45
8: 2*E*, 7*E*	80ºC, 19 h	40% (89% conv)	56:45

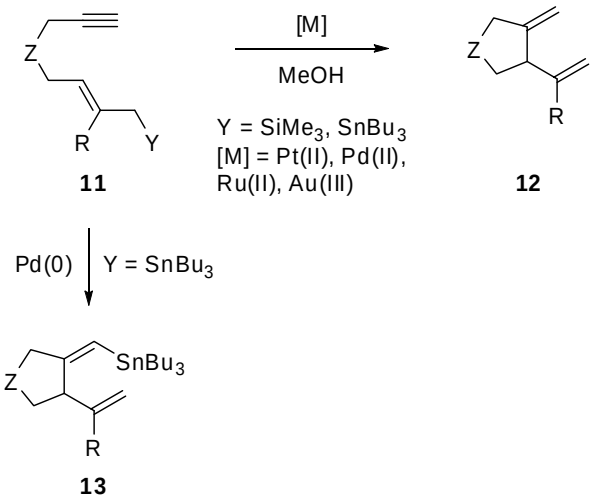
Esquema 4

El empleo de catalizadores de Au(I) permitió extender la reacción a sustratos con distinta funcionalización en el puente y en el alilacetato, pudiéndose aplicar también para la síntesis de compuestos bicíclicos. No obstante, los sustratos precursores del esqueleto de lobanos y lobatrienos no se ciclaron bajo ninguna de las condiciones ensayadas con complejos de Au(I). El mecanismo de la reacción con Au(I) se desconoce por el momento aunque se proponen dos posibles alternativas. La primera, es que la reacción tenga lugar vía transmetalación con el alilestannano formándose un complejo de aliloro(I) intermedio que atacaría como nucleófilo al alilacetato en una reacción de tipo S_N2', dando lugar al producto de ciclación. La otra alternativa es que el complejo

de Au(I) actúe como simple ácido de Lewis coordinándose al acetato y promoviendo un ataque S_N2' del estannano sobre el alilacetato.

Capítulo 2.

Como segunda parte de esta Tesis Doctoral y también dentro del contexto del desarrollo de nuevas reacciones de ciclación catalizadas por metales de transición, se abordó el estudio de ciclaciones de alilestannanos con alquinos. Este tipo de ciclaciones tenían precedente dentro de nuestro grupo de investigación,[4,2] y se sabía que sustratos de tipo **11** reaccionan en presencia de Pt(II), Cu(I), Ru(II) o Au(III) para dar hetero- o carbociclos (**12**) de acuerdo con el esquema **5**, mientras que con Pd(0) dan lugar a estannil derivados (**13**) con configuración definida (*Z*).[5]

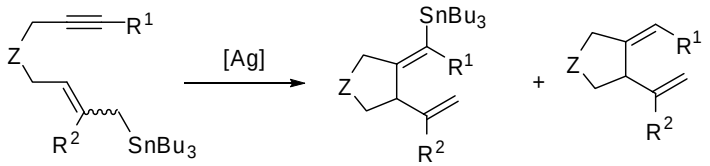


Esquema 5

Se encontró que compuestos de Ag(I) dan lugar estereoselectivamente a productos de tipo **13** pero con configuración contraria en el alqueno (Esquema 6). En este caso, la configuración de la olefina en el alilestannano no afecta a la reacción y sustratos con configuración *E* o *Z* en el alilestannano, reaccionan de la misma manera. Junto con el producto de cicloisomerización **15**, en algunas ocasiones se observó la formación de productos de destannilación **16**.

4 (a) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222. (b) Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren A. M. *J. Org. Chem.* **2002**, *67*, 5197-5201.

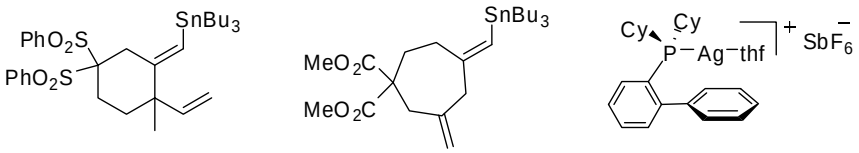
5 Martín-Matute, B.; Buñuel, E.; Méndez, M.; Nieto-Oberhuber, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Organomet. Chem*. **2003**, *687*, 410-419.



14 **15** **16**

Esquema 6

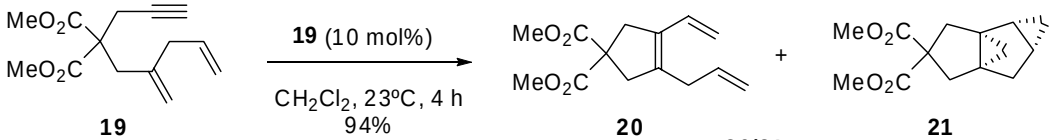
La reacción tiene lugar con sustratos en los cuales Z = $C(CO_2Me)_2$, $C(SO_2Ph)_2$, $C(CH_2OTBPS)_2$, $C(CH_2OH)_2$ y R^1 = H, Ph, R^2 = H, Me con rendimientos comprendidos entre 50-93%, y con tiempos de reacción que oscilan entre 0.5 y 2.5 h. Además se pudo extender a la obtención de ciclos de 6 y 7 miembros como **17** y **18** (Figura 1). Para la obtención de estos compuestos fue necesario el empleo del catalizador de plata **19** cuya estructura fue confirmada por rayos X.



17 (51%) **18** (90%) **19**

Figura 1

El empleo de complejos de Ag(I) con ligandos quirales permitió obtener excesos enantioméricos del 78% en la ciclación de compuestos de tipo **14**, cuando el catalizador empleado es [$(AgOTf)_2$Tol-binap].[6] Además se observó que sales de Ag(I) también reaccionan con 1,6-eninos para dar productos de transposición de esqueleto y de ciclopropanación similares a los obtenidos con Au(I) (Esquema 7).[7] Estos resultados indican que en las ciclaciones de 1,6-eninos intervienen carbenos de Ag(I), y sugieren que también podrían estar involucrados en las ciclaciones de alilestannanos-alilacetatos.



19 **20** **21**

20/21 15:1

Esquema 7

6 Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc*. **2004**, *126*, 5360-5361.

7 (a) Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Cárdenas, D. J.; Buñuel, E.; Nevado, C.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2005**, *44*, 6146-6148. (b) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Eur. J*. **2006**, *12*, 5916-5923.

Abbreviations and acronyms

In this manuscript, the most commonly used abbreviations and acronyms in organic and organometallic chemistry have been applied following the recommendations of: "Guidelines for authors" *J. Org. Chem*. **2007**, *70*, 13A.-27A. Additionally, I have also used the following ones:

binap:	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
cod:	cyclooctadiene
Cy:	cyclohexyl
dba:	dibenzylideneacetone
deguphos:	bis(diphenylphosphino)-1-benzylpyrrolidine
dtbpf:	(di-*tert*-butylphosphino)ferrocene
dppe:	1,2-bis(diphenylphosphino)ethane
dppf:	1,1'-bis(diphenylphosphino)ferrocene
dppm:	bis(diphenylphosphino)methane
dppp:	1,2-bis(diphenylphosphino)propane
diop:	O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
norphos:	2,3-bis(diphenylphosphino)bicyclo[2.2.1]hept-5-ene
TBAF:	tetrabutylamonium fluoride
TBDPS:	*tert*-butyldiphenylsilyl
Tol:	tolyl
Xantphos:	9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene

Chapter 1

1

Introduction

The development of efficient methods for C-C bond formation is the most important subject in organic synthesis. This process is most useful and efficient when conducted catalytically. The use of transition metals for a catalytic C-C bond-forming reaction is attractive because the metal can activate selectively the coordinated organic moiety to facilitate the desired reaction. Among the many transition-metal-catalyzed C-C bond-forming reactions, those involving π-allyl metal intermediates represent some of the most versatile methods to create new C-C bonds.[1]

1 (a) Trost, B. M.; Verhoeven, T. R. in *Comprehensive Organometallic Chemistry*; Eds.; Wilkinson, G.; Stone, F. G.; Abel, E. W.; Pergamon: Oxford, **1982**; Vol. 8, pp. 799-938. (b) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, **1985**. (c) Farina, V. in *Comprehensive Organometallic Chemistry II*; Eds.; Wilkinson, G.; Stone, F. G.; Abel, E. W.; Pergamon: Oxford, **1995**; Vol. 12, pp. 161-240. (d) Tsuji, J. *Palladium Reagents and Catalyst*; Wiley: Chichester, **1995**. (e) *Metal-Catalyzed Cross-Coupling Reactions*; Eds.; Diederich, F.; Stang, P. J.; Wiley-VCH: Weinheim, **1988**. (f) Malleron, J.; Fiaud, J.; Legros, J. *Handbook of Palladium-Catalyzed Organic Reactions*; Academic Press: San Diego, **1997**. (g) Negishi, E. *Organopalladium Chemistry*; Wiley-Interscience, New York, **2002**, Vols. I and II.

1. Allyl complexes

An allyl ligand, C_3R_5, can coordinate to a transition metal in three limiting ways (Figure 1): as a σ-bound ligand (**1**), as a σ-π-bound ligand[2] (**2a** and **2b**) or as a fully π-bound ligand (**3**). In the monohapto form (**1**) it is a simple 1-electron X-type ligand like Me, while in the trihapto forms (**2a**, **2b** and **3**) it acts as a 3-electron LX enyl ligand. Complexes **2a** and **2b** can be considered as resonance forms of **3**.

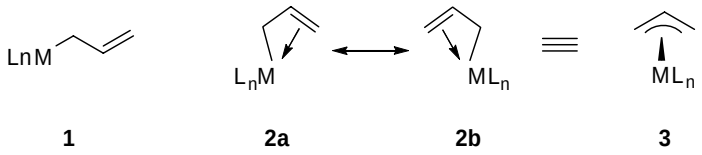


Figure 1

The manner in which allyl ligands are coordinated and their ability to change their coordination geometries depend on the metal center. In the majority of the applications for catalytic reactions, the geometry is η^3-allyl. Substituents on allylic ligands are traditionally named according to their configuration relative to the substituent at C-2 (Figure 2). The substituents which are *syn* to H-2 are designated as "*syn*"; the substituents *anti* to H-2 are labelled as "*anti*".

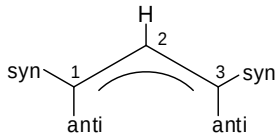
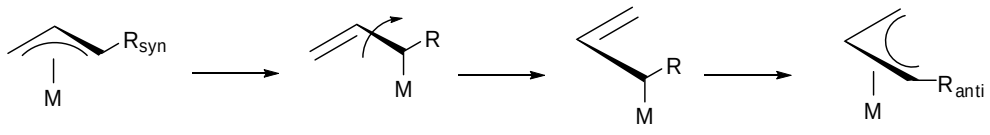


Figure 2

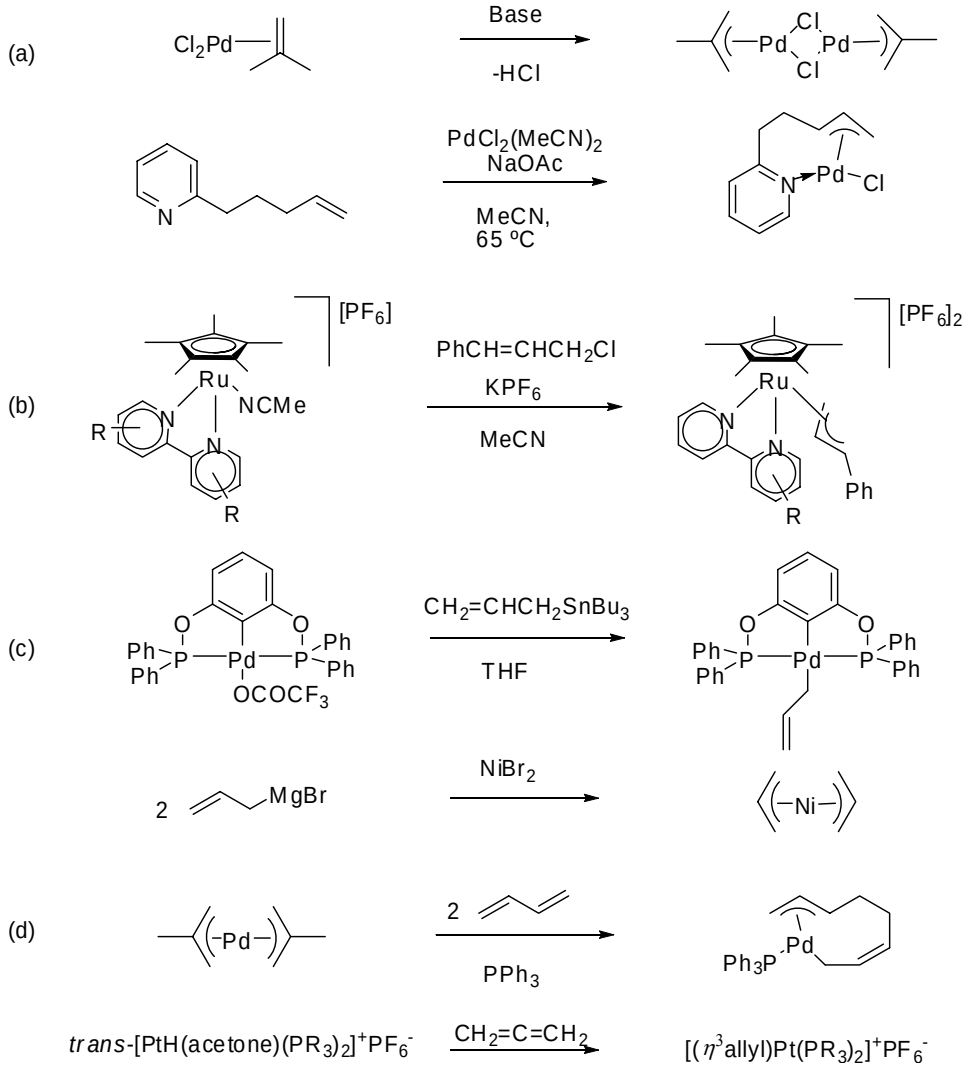
The η^3-allyl group often shows exchange of the *syn* and *anti* substituents. The mechanism goes through an η^1-allyl intermediate as shown in Scheme 1. This kind of ligand exchange means that an allyl complex of a given configuration may rearrange in time.



Scheme 1

2 Carturan, G.; Belluco, U.; Del Pra, A.; Zanotti, G. *Inorg. Chim. Acta* **1979**, *33*, 155-160.

Allylic complexes can be synthesized by: (a) allylic deprotonation of coordinated olefins,[3] (b) electrophilic attack of allylic compounds to metals,[4] (c) nucleophilic attack of allylic compounds to metals,[5] (d) reaction with dienes or allenes.[6] Some examples are depicted in Scheme 2.



Scheme 2

3 (a) Smidt, J.; Hafner, W. *Angew. Chem*. **1959**, *71*, 284. (b) Hüttel, R.; Kratzer, J. *Angew. Chem*. **1959**, *71*, 456. (c) Chengebroyen, J.; Grellier, M.; Pfeffer, M. *Eur. J. Inorg. Chem*. **1998**, 1563-1571.

4 Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Angew. Chem. Int. Ed*. **2003**, *42*, 5066-5068.

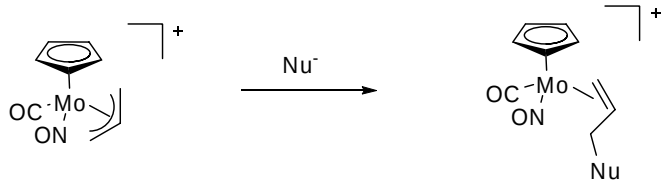
5 (a) Solin, N.; Kjellgren, J.; Szabó, K. J. *J. Am. Chem. Soc*. **2004**, *126*, 7026-7033. (b) Wilke, G.; Bogdanovic, B. *Angew. Chem*. **1961**, *73*, 756.

6 (a) Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, B. Schenker, G.; Schick, K.-P.; Schroth, G. *Organometallics* **1985**, *4*, 1945-1953. (b) Clark, H. C.; Kurosawa, H. *Inorg. Chem*. **1972**, *11*, 1275-1280.

Routes b and c are the synthetic methods most commonly used for allyl complexes. Example d shows that allenes insert into an M-H bond to place the hydride on the central carbon and generate an allyl group.

Generally, η^3-allyl transition metal complexes can function as either electrophilic or nucleophilic allylating agents, depending on the properties of the transition metal and the coordinated ligands. The most important reactions of allyls are shown bellow.

1. Reaction with nucleophiles:[7]



2. Reaction with electrophiles:[8]

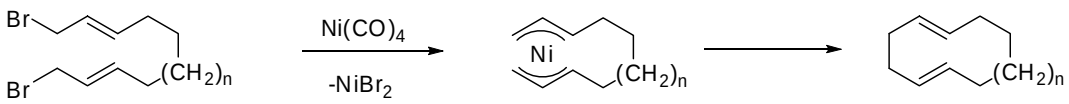
$$Cp(CO)_2FeCH_2CH{=}CH_2 + E^+ \longrightarrow [Cp(CO)_2FeCH_2CH{=}CH_2E]^+$$

$E^+ = HgCl^+, Me^+, RCO^+, H^+, Br^+$

3. Insertion:[9]

$$(\eta^3\text{-allyl})_2Ni \xrightarrow{CO_2} (\eta^3\text{-allyl})NiOCOCH_2CH{=}CH_2$$

4. Reductive elimination:[10]



7 Adams, R. D.; Chodosh, D. F.; Faller, J. W.; Rosan, A. M. *J. Am. Chem. Soc*. **1979**, *101*, 2570.

8 Rosenblum, M. *Acc. Chem. Res*. **1974**, *7*, 125.

9 Tsuda, T.; Chujo, Y.; Saegusa, T. *Synth. Comun*. **1979**, *9*, 427-430.

10 Corey, E. J.; Semmelhack, M. F. *Tetrahedron Lett*. **1966**, *7*, 6237-6240.

1.1. Catalyzed allylation reactions

1.1.1. Nucleophilic addition to π-allyl complexes: allylic substitution

For a π-allyl complex with electrophilic character the most common and general reaction is the allylic substitution (or allylic alkylation) by different nucleophiles. Transition metal catalyzed allylic substitution provides a powerful tool for the construction of complex molecules, and hence is the focus of intense synthetic attention.[1d,11] Many recent efforts in this area have been centered on developing catalysts that enable high regio- and stereochemical control in the substitution reaction of symmetrical and unsymmetrical substrates. Irrespective of the structure of the starting materials (e.g., **4** or **5,** Figure 3), palladium catalyzed processes typically favour nucleophilic substitution at the sterically less hindered allylic terminus to give **6**,[1e] whereas Ru[12], Mo[13], Rh[14], Ir[15] and W[16] prefentially yield products **7** arising from attack at the more encumbered allylic terminus.

11 For a review on catalytic allylic substitutions, see: (a) Helmchen, G.; Dahnz, A.; Dübon, P.; Schelwies, M.; Weihofen, R. *Chem. Commun*. **2007**, 675-691. (b)Yorimitsu, H.; Oshima, K. *Angew. Chem. Int. Ed*. **2005**, *44*, 4435-4439. (c) Helmchen, G.; Ernst, M.; Paradies, G. *Pure Appl, Chem*. **2004**, *76*, 495-506. (d) Graening, T.; Schmalz, H.-G. *Angew. Chem. Int. Ed*. **2003**, *42*, 2580-2584. (e) Trost, B. M.; Van Vranken, D. L. *Chem. Rev*. **1996**, *96*, 395-422. (f) Hayashi, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: Weinheim, **1993**; p 325. (g) Frost, C. G.; Howarth, J.; Williams, J. M. *Tetrahedron: Asymmetry.* **1992**, *3*, 1089-1122. (h) Consiglio, G.; Waymouth, M. *Chem. Rev*. **1989**, *89*, 257-276.

12 (a) Ono, H.; Satake, N.; Watanabe, Y. *Organometallics* **1995**, *14*, 1945. (b) Morisaki, Y.; Kondo, T.; Mitsudo, T. *Organometallics* **1999**, *18*, 4742. (c) Trost, B. M.; Fraisse, P.; Ball, Z. *Angew. Chem. Int. Ed*. **2002**, *41*, 1059. (d) Hermatsheweiler, R.; Fernández, I.; Breher, F.; Pregosin, P. S.; Veiros, L. F.; Calhorda, M. *Angew. Chem. Int. Ed*. **2005**, *44*, 4397-4400. (e) Bruneau, C.; Renaud, J.-L.; Demerseman, B. *Chem. Eur. J*. **2006**, *12*, 5178-5187.

13 (a) Trost, B. M.; Merlic, C. *J. Am. Chem. Soc*. **1990**, *112*, 9590-9600. (b) Trost, B. M.; Hildbrand, S.; Dogra, K. *J. Am. Chem. Soc*. **1999**, *121*, 10416-10417. (c) Kaiser, N. F.; Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *Angew. Chem. Int. Ed*. **2000**, *39*, 3595-3598.

14 (a) Minami, I.; Shimizu, I.; Tsuji, J. *J. Organomet. Chem*. **1985**, *296*, 269-280. (b) Evans, P. A.; Nelson, J. D. *Tetrahedron Lett*. **1998**, *39*, 1725-1728. (c) Evans, P. A.; Kennedy, L. J. *J. Am. Chem. Soc*. **2001**, *123*, 1234-1235. (d) Prétôt, R.; Pfaltz, A. *Angew. Chem. Int. Ed*. **1998**, *37*, 323-325. (e) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc*. **1998**, *120*, 5581-5582. (f) Selvakumar, K.; Valentini, M.; Pregosin, P. S.; Albinati, A. *Organometallics* **1999**, *18*, 4591-4597. (g) Hayashi, T.; Okada, A. Suzuka, T.; Kawatsura, M. *Org. Lett*. **2003**, *5*, 1713-1715. (e) Evans, P. A.; Leathy, D. K.; Slieker,

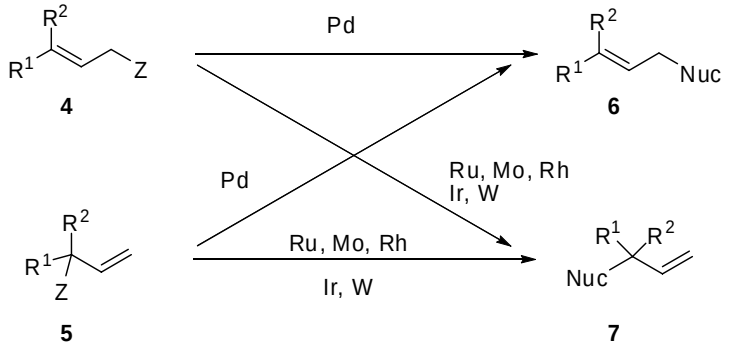


Figure 3

These reactions are generally believed to proceed via a transition metal stabilized allyl intermediate that may vary in structure from an unsymmetrical η^1complex to a symmetrical η^3-allyl complex. The regioselectivity of the ensuing nucleophilic attack is then dictated by a combination of steric and electronic factors that vary with the intermediate complex and the nucleophile.[17]

1.1.1.1. Palladium catalyzed allylic substitution

Of the various transition metals used, palladium is the one who has been most extensively studied and the one who has led to a major number of applications. The palladium catalyzed allylic substitution is known as the Tsuji-Trost reaction.[1a,1d,18] The

L. M. *Tetrahedron: Asymmetry* **2003**, *14*, 3613-3618. (f) Ashfeld, B. L.; Miller, K. A.; Martin, S. F. *Org. Lett*. **2004**, *6*, 1321-1324. (g) Evans, P. A.; Leathy, D. K.; Andrews, W. J.; Uraguchi, D. *Angew. Chem. Int. Ed*. **2004**, *43*, 4788-4791 (h) Menard, F.; Chapman, T. M.; Dockendorff, C.; Lautens, M. *Org. Lett*. **2006**, *8*, 4569-4572.

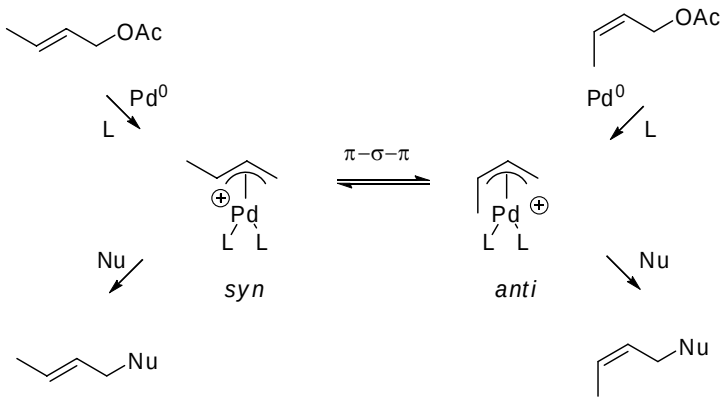
15 (a) Takeuchi, R.; Kashio, M. *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 263-265. (b) Janssen, G.; Helmchen, G. *Tetrahedron Lett*. **1997**, *38*, 8025-8026. (c) Bartels, B.; Helmchen, G. *Chemm. Commun*. **1999**, 741-742. (d) Takeuchi, R.; Tanabe, K. *Angew. Chem. Int. Ed*. **2000**, *39*, 1975-1978. (e) Hemchen, G.; Dahnz, A.; Dübon, P.; Schelwies, M.; Weihofen, R. *Chem. Commun*. **2007**, 675-691.

16 (a) Trost, B. M.; Hung, M.-H. *J. Am. Chem. Soc*. **1983**, *105*, 7757-7759. (b) Lloyd-Jones, G. C.; Ptaltz, A. *Angew. Chem. Int. Ed. Engl*. **1995**, *34*, 462-464. (c) Malkov, A. V.; Baxendale, I. R.; Dvořák, D.; Mansfiel, D. J.; Kočovský, P. *J. Org. Chem*. **1999**, *64*, 2737-2750.

17 Trost, B. M.; Hung, M.-H. *J. Am. Chem. Soc*. **1984**, *106*, 6837-6839.

18 (a) Godleski, S. A. in *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, **1991**; Vol. 4, pp. 585-661. (b) Heumann, A.; Réglier, M. *Tetrahedron*, **1995**, *51*, 975-1015. (c) Harrington, P. J. in *Comprehensive Organometallic Chemistry*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon: Oxford, **1982**; Vol 12, Chapter 8.2, pp. 797-904. (d) Tsuji, J. *Transtion Metal Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: Chichester,

reaction work as follows: the oxidative addition of palladium(0) to (*E*)-allyl acetates and carbonates leads to *syn*-configured allyl complexes (Scheme 3), which react with nucleophiles (Nu) to provide the corresponding *E*-substitution products. The *anti* complexes are generated by the attack of palladium on *Z* substrates. Subsequent reaction with nucleophiles should result in *Z*-configured products. The energy barrier for the π-σ-π isomerisation in Pd-allyl complexes is low and isomerisation takes place with preference for the *syn* complex that is more stable. Exceptions can only be observed if steric interactions either between the substituents in the allylic substrate[19] or between the allyl moiety and the ligands on the palladium[20] destabilize the *syn* complex. As a result, *trans* olefins are obtained in most of the cases. Nonetheless, there are a few examples where the nucleophilic attack is faster than the isomerisation reaction leading to products in which the olefin geometry of the starting material is retained.[21]



Scheme 3

The fast π-σ-π isomerisation process also affects the regioselectivity of the reaction so that when monosubstituted allylic substrates are submitted to the reaction, branched and linear substrates afford the same intermediate. The regiochemistry in the

2000, pp. 109-168. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev*. **2003**, *103*, 2921-2944. (c) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res*. **2000**, *33*, 336-345.

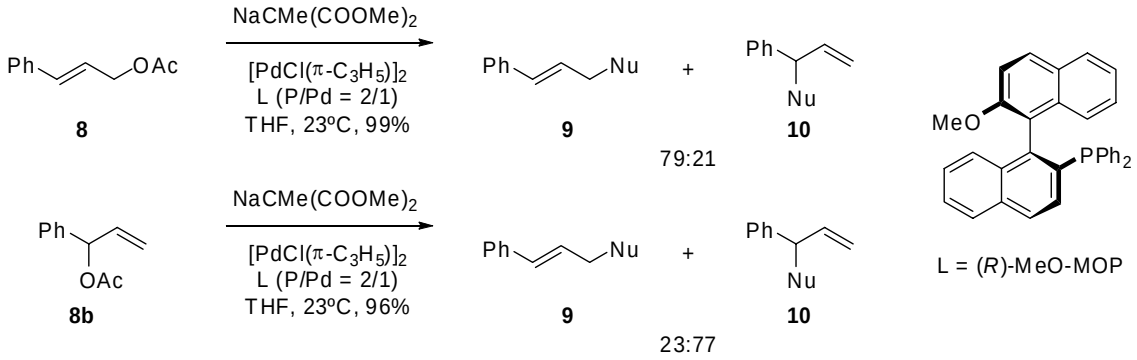
19 (a) Faller, J. W.; Thomsen, M. E.; Mattina, M. J. *J. Am. Chem. Soc*. **1971**, *93*, 2642-2653. (b) Lukas, J.; Ramakers-Blom, J. E.; Hewitt, T. G.; De Boer, J. J. *J. Organomet. Chem*. **1972**, *46*, 167-177.

20 (a) Åkermark, B.; Hansson, S.; Vitagliano, A. *J. Am. Chem. Soc*. **1990**, *112*, 4587-4588. (b) Sjögren, M.; Hansson, S.; Norrby, P.-O.; Åkermark, B.; Cucciolito, M. E.; Vitagliano, A. *Organometallics* **1992**, *11*, 3954-3964.

21 (a) Huntsinger, M. W.; Oehlschlager, A. C. *J. Org. Chem.* **1991**, *56*, 2918-2920. (b) Sjogren, M. P. T.; Hansson, S.; Akermark, B. *Organometallics* **1994**, *13*, 1963-1971. (c) Kazmaier, U.; Zumpe, F. L. *Angew. Chem. Int. Ed*. **2000**, *39*, 802-804.

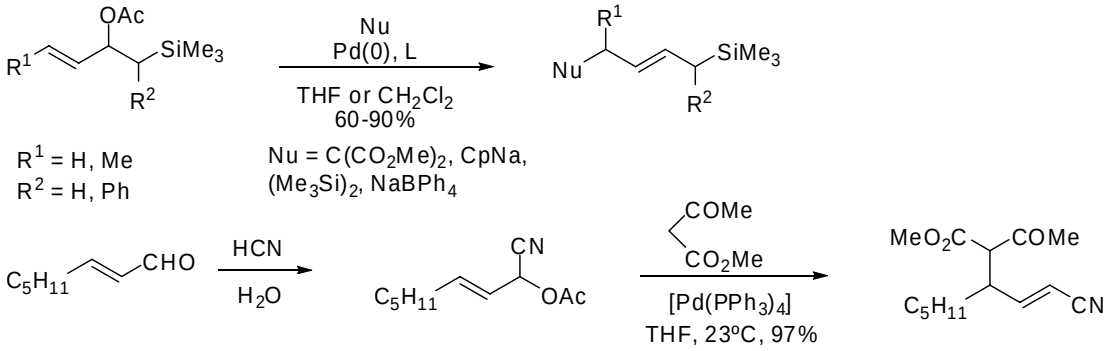
substitution products is thus determined by the attack of the nucleophile which prefers the less hindered terminal position affording linear products with high regioselectivity.

Exceptional regioselectivity depending on the substrates and ligands has been reported. Hayashi found that regiochemistry of allylation of $NaCMe(CO_2Me)_2$ with allyl acetates **8a** and **8b** is partially retained in the final products **9** and **10** when bulky ligands are used (Scheme 4).[22] Substitution took place with preference at the position originally occupied by the leaving acetate. This is an example of a memory effect. A similar memory effect of π-allylic ligands was observed by Acemoglu and Williams in the reaction of allyl acetates when bulky aliphatic phosphines, tipically tricyclohexylphosphine, were used.[23]



Scheme 4

Unsymetrically 1,3-substituted allylic substrates often react with low regioselectivity, nevertheless this can be solved by introducing directing substituents like heteroatoms or electron withdrawing groups (Scheme 5).[24]



Scheme 5

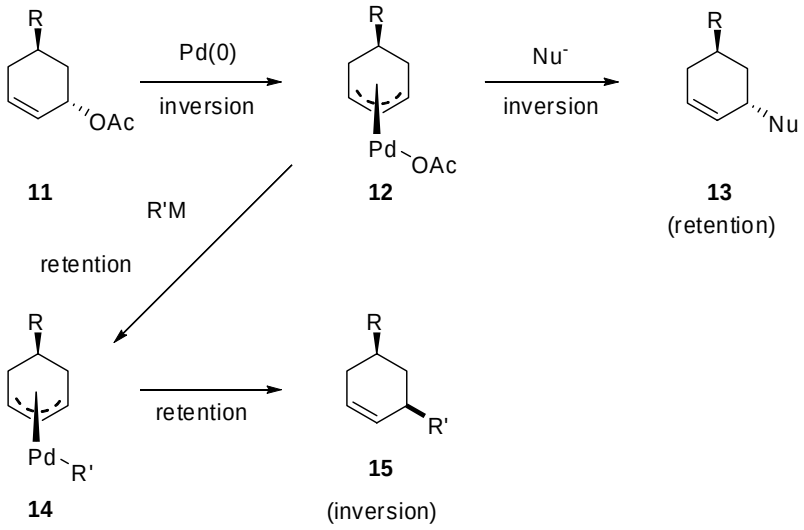
22 Hayashi, T.; Kawatsura, M.; Uozumi, Y. *J. Am. Chem. Soc*. **1998**, *120*, 1681-1687.

23 Acemoglu, L.; Williams, J. M. J. *Adv. Synth. Catal*. **2001**, *343*, 75-77.

24 (a) Macsári, I.; Hupe, E.; Szabó, K. J. *J. Org. Chem.* **1999**, *64,* 9547-9556. (b) Tsuji, J.; Ueno, H.; Kobayshi, Y.; Okumoto, H. *Tetrahedron Lett*. **1981**, *22*, 2572-2574.

Additionally, under special reaction conditions, regioselective nucleophilic attack at the central carbon of the allyl ligand has been achieved.[25]

The stereochemistry of the reaction has been studied extensively. Starting from allyl acetate **11**, formation of π-allylpalladium complex **12** proceeds with inversion of configuration (*anti* attack). Subsequent reaction of **12** with nucleophiles occurs with different stereochemistry depending on the nature of the nucleophiles. Soft (stabilized) nucleophiles, which are derived from conjugated acids with pK_a < 25, such as active methylene compounds, attack **12** from the backside of the Pd atom to give **13** with inversion of stereochemistry. Thus, overall retention is observed. On the other hand, hard nucleophiles (pK_a > 25), typically organometallic compounds of main group metals (Mg, Zn, B, Sn and others), generate **14** by transmetalation, and subsequent reductive elimination affords **15**. Both the transmetalation and reductive elimination proceed with retention, and hence overall inversion is observed with hard nucleophiles.



Scheme 6

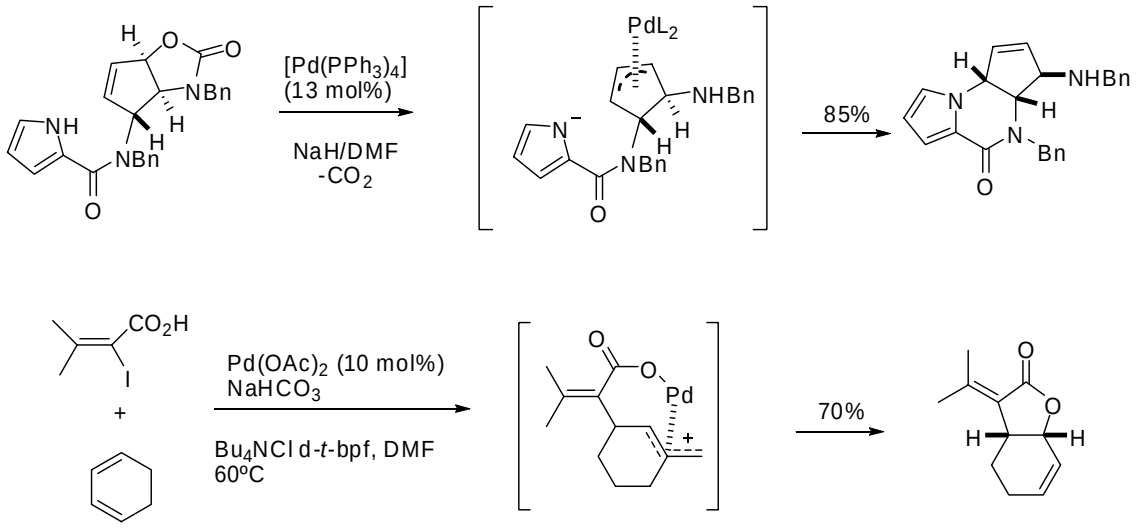
However, Kurosawa and co-workers observed both inversion and retention of configuration in the oxidative addition of 5-(methoxycarbonyl)-2-cyclohexenyl chloride to Pd(0) depending on the ligands and solvents used.[26]

25 (a) Carfagna, C.; Mariano, L.; Musco, A.; Sallese, G.; Santi, R. *J. Org. Chem*. **1991**, *56*, 3924-3927. (b) Aranyos, A.; Szabó, K. J.; Castaño, A. M.; Bäckvall, J. *Organometallics*, **1997**, *56*, 3924-3927. (c) Satake, A.; Nakata, T.; *J. Am. Chem. Soc*. **1998**, *120*, 10391-10396. (d) Satake, A.; Koshino, H.; Nakata, T. *Chem. Lett*. **1999**, 49-50.

26 Kurosawa, H.; Kajimary, H.; Ogoshi, S.; Yoneda, H.; Miki, K.; Kasai, N.; Murai, S.; Ikeda, I. *J. Am. Chem. Soc*. **1992**, *114*, 8417-8424.

Many allylic compounds can be used as substrates and in most of the cases the use of a base is required to generate the anionic nucleophile. Nevertheless, the use of allylic carbonates[27] or allylic epoxides[27g,28] as electrophiles offers the possibility of carrying out the reaction under neutral conditions due to the *in situ* generation of an alkoxide, which acts as a catalytic base deprotonating the protonucleophile.

Intamolecular palladium catalyzed allylic alkylations enable the synthesis of a wide range of carbo- and heterocyclic systems, often in a regio- and diastereoselective manner. The number of control elements present in cyclizations of this nature allows fine-tunning of the reactivity. Two representative examples of the potential of this method for ring construction are depicted in Scheme 7.[29]



Scheme 7

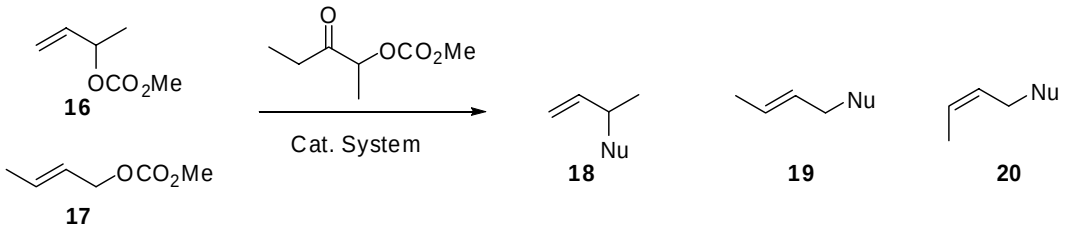
27 (a) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809-4812. (b) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugigura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50,* 1523-1529. Reviews: (c) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140-145. (d) Tsuji, J. *Tetrahedron* **1985**, *42*, 4361-4401. (e) Castaño, A.; Echavarren, A. M. *Tetrahedron Lett*. **1996**, *36*, 6587-6590. (f) Castaño, A.; Ruano, M.; Echavarren, A. M. *Tetrahedron Lett*. **1996**, *37*, 6591-6594. (g) Castaño, A. M.; Méndez, M.; Ruano, M.; Echavarren, A. M. *J. Org. Chem*. **2001**, *66*, 589-593.

28 (a) Tueting, D. R.; Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039-4040. (b) Tueting, D. R.; Echavarren, A. M.; Stille, J. K. *Tetrahedron,* **1989**, *45*, 979-992. (c) Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22,* 2575-2578. (d) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969-5971. (e) Trost, B. M.; Warner, R. W. *J. Am. Chem. Soc.* **1983**, *105*, 5940-5942. (f) Trost, B. M.; Granja, J. R. *J. Am. Chem. Soc.* **1991**, *113,* 1044-1046. (g) Blart, E.; Genêt, J. P.; Safi, M.; Savignac, M.; Sinou, D. *Tetrahedron* **1994**, *50,* 505-514.

29 For a recent review: Hyland, C. *Tetrahedron* **2005**, *61*, 3457-3471.

1.1.1.2 Rhodium and other late transition metals as catalysts for allylic substitution

Rhodium catalysts have some unique features in the allylic alkylation reactions. Back in 1985 Tsuji et al. compared the Rh- and Pd-catalyzed allylic alkylations of β-keto esters using allylic substrates **16** and **17** (Scheme 8).[30] With Pd, the product distribution was nearly independent of the used substrate, while the Rh-catalyzed reaction provided preferentially the product in which the incoming substituent takes the position of the previous leaving group. They found that the Pd-catalyzed reaction proceeds faster and under milder conditions than the Rh-catalyzed reaction.



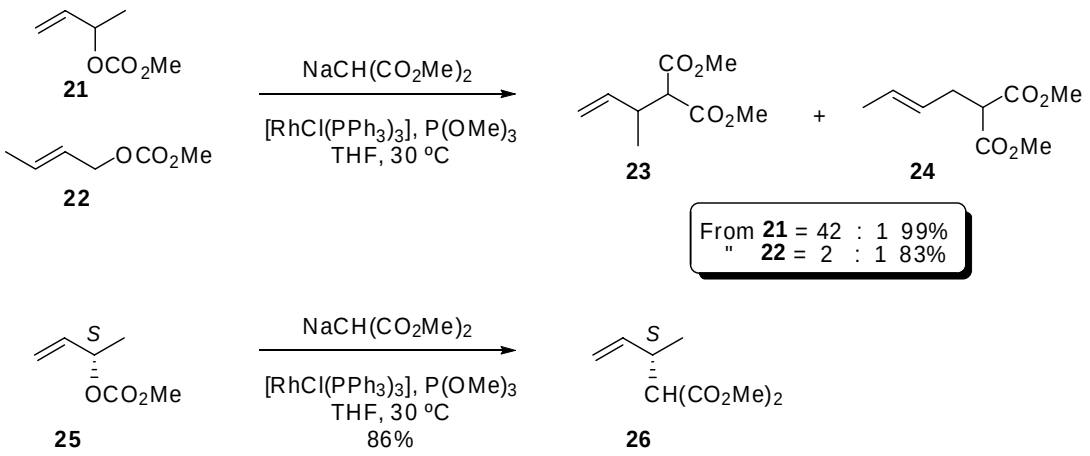
Cat. System	Substrate	Yield [%]	18 : 19 : 20
$[Pd_2(dba)_3]\cdot CHCl_3$	**16**	89	27 : 65 : 8
THF, 23°C, 0.5 h	**17**	93	29 : 63 : 8
$[RhH(PPh_3)_4]$, $P(n\text{Bu})_3$	**16**	81	86 : 12 : 2
dioxane, 100°C, 2 h	**17**	97	28 : 63 : 9

Scheme 8

Later, the groups of Evans and Takeuchi recognized that phosphite ligands significantly improve the reaction rate as well as the regioselectivity.[31] As phosphites are better π acceptors than phosphanes the resulting rhodium-allyl intermediates are more electrophilic, and nucleophilic attack occurs preferentially at the sterically more hindered position. If optically active substrates such us **25** are used, the chiral information can be transferred to the product (Scheme 9). This is not possible with Pd catalysts because of the very fast π-σ-π isomerization. With soft nucleophiles the reaction proceeds with overall retention, suggesting a double inversion process.[31b]

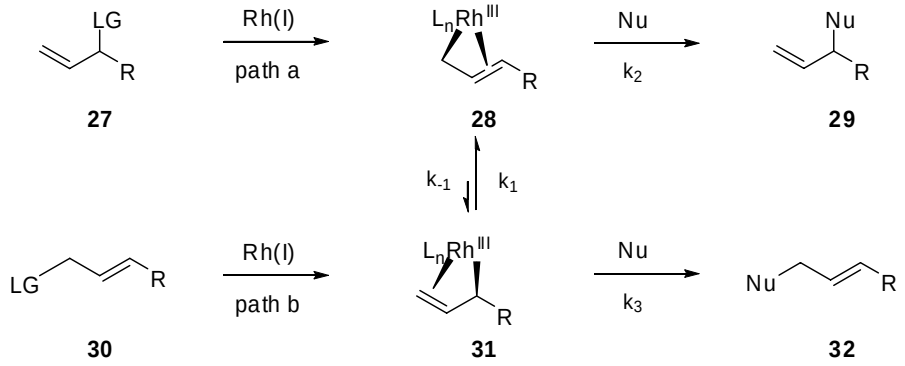
30 Minami, I.; Shimizu, I.; Tsuji, *J. Organomet. Chem*. **1985**, *296*, 269-280.

31 (a) Nelson, J. D.; Evans, P. A. *Tetrahedron Lett*. **1998**, *39*, 1725-1728. (b) Nelson, J. D.; Evans, P. A. *J. Am. Chem. Soc*. **1998**, *120*, 5581-5582. (c) Takeuchi, R.; Kitamura, N. *New J. Chem*. **1998**, 659-660.



Scheme 9

The high regio- and stereoselectivity observed in the rhodium-catalyzed system was explained according to the mechanism depicted in Scheme 10. In path a, treatment of the secondary allylic system **27** with rhodium gives the enyl intermediate **28**, which in the presence of a nucleophile undergoes a rapid S_N2' displacement, which is faster than isomerisation to **31** ($k_2 > k_{-1}$). The formation of the enyl species explains the retention of stereochemistry. In path b, initial oxidative addition into the primary allylic system **30** furnishes the isomeric enyl **31** in competition with alkylation ($k_1 > k_3$), leading to a mixture of **32** and **29**.



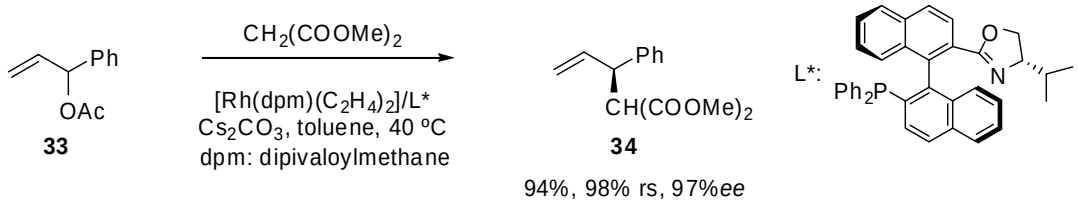
Scheme 10

Later it was discovered that $[RhCl(CO)_2]_2$ catalyzes allylic alkylation under mild and ligandless conditions.[32] With this catalyst, reactions involving unsymmetrical substrates, including those with internal double bonds, proceed efficiently and regioselectivity at the carbon atom bearing the leaving group (memory effect). The substitution also proceeds stereoselectively with retention of double-bond geometry and

32 Ashfeld, B. L.; Miller, K. A.; Martin, S. F. *Org. Lett*. **2004**, *6*, 1321-1324.

allylic chirality. This is significant as (*Z*)-allylic substrates generally suffer extensive *E*-*Z* isomerisation with other transition metal catalysts.

The tendency for interconversion of the rhodium-allyl complexes seems to depend on the substrate used. Pregosin et al.[33] and Hayashi et al.[34] demonstrated that under suitable conditions, racemic aryl-substituted substrates **33** can be converted into nearly enantiomerically pure products **34** in the presence of chiral ligands (Scheme 11). This clearly indicates that π-σ-π isomerisation can also occur in Rh complexes and that the Rh-catalyzed allylic alkylation is considerably less well understood than the Pd-catalyzed version.



Scheme 11

Rhodium catalysts are also useful to performed allylic alkylation with less commonly used unstabilized nucleophiles. The use of these nucleophiles is limited to symmetrical or stereoelectronically biased allyl fragments to circumvent problems associated with pour regiochemistry. Nonetheless, the alkali metal salts of enolates,[35] fenols,[36] alcohols,[35b,37] and *N*-(arylsulfonyl)anilines[38] have been successfully used as partners in the rhodium-catalyzed allylic substitution.

Alkali metal alkoxides and enolates were transmetalated with copper(I) salts to soften the basic character and avoid extensive side reactions. By this method, not only primary, but also secondary, and tertiary alcohols can be used as suitable substrates for allylic etherification (Scheme 12).[37a]

33 Selvakumar, K.; Valentini, M.; Pregosin, P. S.; Albinati, A. *Organometallics* **1999**, *18*, 4591-4597.

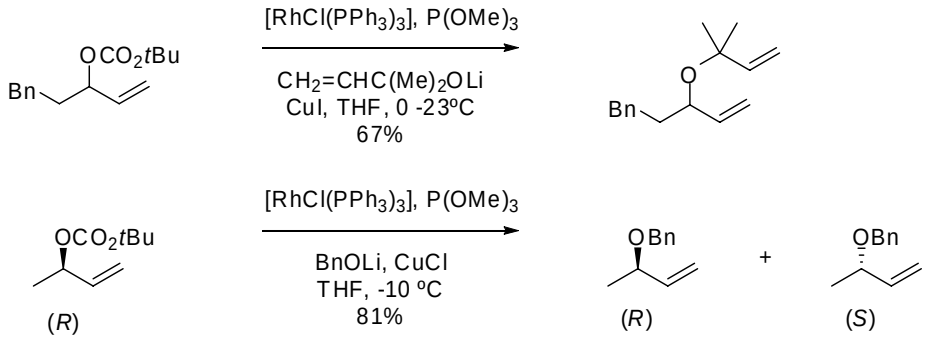
34 Hayashi, T.; Okada, A.; Suzuka, T.; Kawatsura, M. *Org. Lett*. **2003**, *5*, 1713-1715.

35 (a) Evans, P. A.; Leahy, D. K. *J. Am. Chem. Soc*. **2003**, *125*, 8974-8975. (b) Evans, P. A.; Leahy, D. K.; Slieker, L. M. *Tetrahedron: Asymmetry* **2003**, *14*, 3613-3618. (c) Kazmaier, U.; Stolz, D. *Angwe. Chem. Int. Ed*. **2006**, *45*, 3072-3075.

36 Evans, P. A.; Leahy, D. K. *J. Am. Chem. Soc*. **2000**, *122*, 5012-5013.

37 (a) Evans, P. A.; Leahy, D. K. *J. Am. Chem. Soc*. **2002**, *124*, 7882-7883. (b) Evans, P. A.; Leahy, D. K.; Andrews, W. J.; Uraguchi, D. *Angwe. Chem. Int. Ed*. **2004**, *43*, 4788-4791.

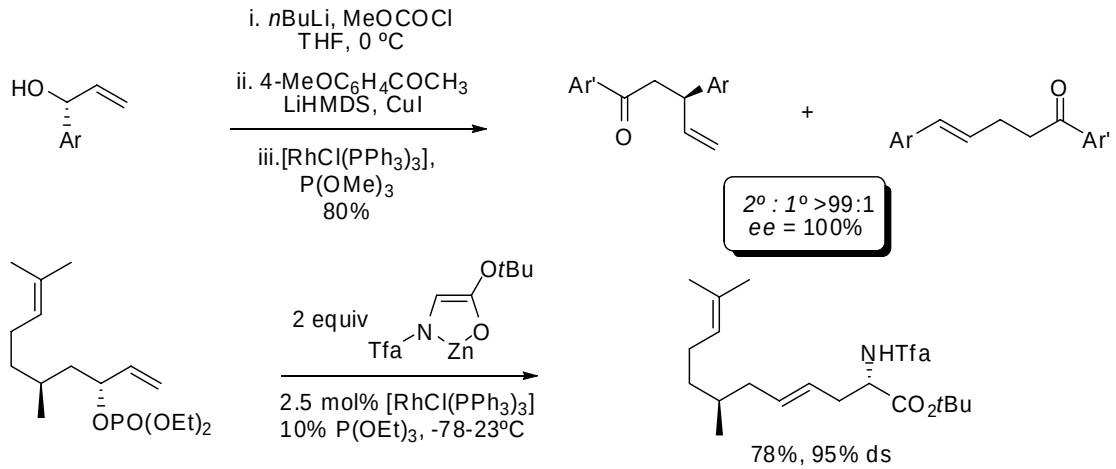
38 Evans, P. A.; Robinson, J. E.; Moffett, K. K. *Org. Lett*. **2001**, *3*, 3269-3271.



Scheme 12

The choice of the copper(I) salt was crucial for obtaining high stereospecificity and regioselectivity. Interestingly, the trend for enantiospecificity was the reverse of that for regiospecificity. Although the best regioselecivities were obtained by employing CuI, the iodine anion led to poor enantiospecificity while chlorine gave the best. This observation was attributed to the *trans*-effect, by virtue of an *in situ* modification of the catalyst by the halide ion.

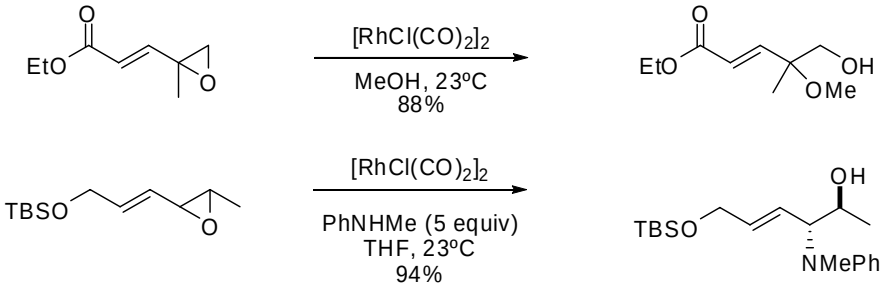
The concept of modulating the reactivity of a nucleophile through the transmetalation with a copper(I) halide was extended to enolates with good results.[35a,b] Also chelated enolates obtained from amino acid esters[35c] have been successfully applied as nucleophiles for Rh-catalyzed allylic alkylation. Owing to their high reactivity, these enolates react under much milder conditions with excellent chirality transfer and high regioselectivities (Scheme 13).



Scheme 13

$[RhCl(CO)_2]_2$ catalyzes the ring opening of vinyl epoxides with alcohols and aromatic amines to give 1,2-additon products. Transition metal catalyzed reactions giving 1,2-addition products are far fewer in number. These substrates can sometimes

be obtained through stoichiometric or catalytic use of Brønsted and Lewis acids, but these methods suffer from poor functional group compatibility. $[RhCl(CO)_2]_2$ is an effective catalyst and can perform the reaction under neutral conditions at room temperature.[39]



Scheme 14

The catalytic activity of ruthenium complexes was first shown in 1985 by Tsuji, who used the ruthenium(II) dihydride complex $[RuH_2(PPh_3)_4]$ to perform the substitution of allyl and cinnamyl carbonates by stabilizing carbon nucleophiles arising from β-ketoesters.[40] The first regioselective ruthenium-catalysed reaction with a carbon nucleophile was reported by Mitsudo using [Ru(cod)(cot)] as catalyst for highly regioselective reactions with several carbon nucleophiles. However, no regioselectivity was obtained for the reaction with malonate anion.[41] Trost reported that a branched type of alkylation with malonate anion proceeded with a high selectivity using $[Cp^*Ru(NCCH_3)_3]PF_6$.[12c] Bruneau also reported some ruthenium catalyzed reactions that exhibited a branched-type selectivity,[42,12e] and Pregosin reported examples of a number of π-allylruthenium intermediates that generated branched products.[43,12d]

39 Fagnou, K.; Lautens, M. *Org. Lett*. **2000**, *2*, 2319-2321.

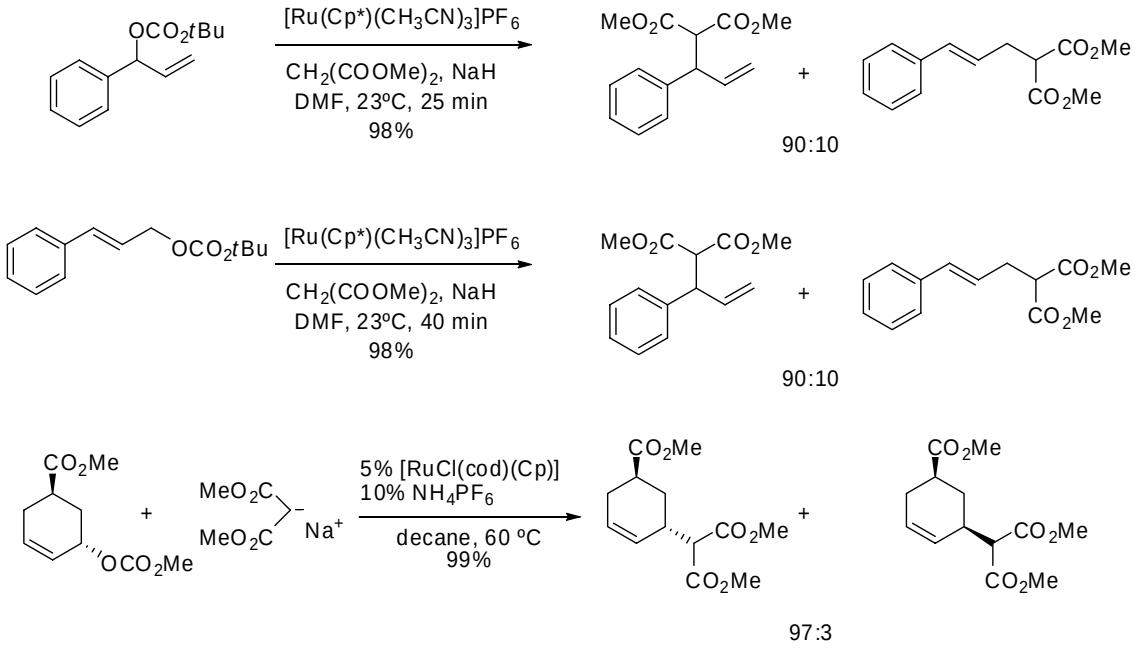
40 Minami, I.; Shimizu, I.; Tsuji, J. *J. Organomet. Chem*. **1985**, *296*, 269-280.

41 Zhang, S.-W.; Mitsudo, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem*. **1993**, *450*, 197-207.

42 (a) Gürbüz, N.; Özdemir, B.; Cetinkaya, B.; Renaud, J.-L.; Demerseman, B.; Bruneau, C. Tetrahedron Lett. **2006**, *47*, 535-538. (b) Mbaye, M. D.; Demerseman, B.; Renaud J.-L.; Bruneau, C. *J. Organomet. Chem*. **2005**, *691*, 2149-2158. (c) Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Adv. Synth. Catal*. **2004**, *346*, 835-841. (d) Mbaye, M. D.; Demerseman, B.; Renaud, J.-L.; Toupet, L.; Bruneau, C. *Angew. Chem. Int. Ed*. **2003**, *42*, 5066-5068. (e) Renaud, J.-L.; Bruneau, C.; Demerseman, B. *Synlett*, **2003**, 408-410.

43 (a) Hermatschweiler, R.; Fernández, I.; Pregosin, P. S.; Breher, F. *Organometallics*, **2006**, *25*, 1440-1441. (b) Fernández, I.; Hermatschweiler, R.; Pregosin, P. S.; Albinati, A.; Rizzato, S. *Organometallics* **2006**, *25*, 323-330. (c) Hermatschweiler, R.; Fernández, I.; Pregosin, P. S.;

Although the general trend of ruthenium complexes in allylic alkylation has been the formation of branched products, recently Kawatsura and Itoh have reported the first example of a ruthenium catalyzed linear-type of allylic alkylation with a malonate anion.[44] Notably, the addition of malonate to allylic carbonates occurs with retention of the configuration of the original carbonate. This implies a mechanism similar to that for palladium allylic alkylation, involving double inversion of configuration.[45]



Scheme 15

Other transition metals have also been employed in allylic alkylation. Iron behaves as rhodium and ruthenium complexes leading to a high degree of conservation of enantiomeric excess.[46] Molybdenum[13] and wolframium[16] afford branched products with higher levels of both regio- and enantioselectivity. Copper allows the use of hard nucleophiles including Grignard and organozinc reagents with a S_N2'-type

Watson, E. J.; Albinati, A.; Rizzato, S.; Veiros, L. F.; Calhorda, M. J. *Organometallics* **2005**, *24*, 1809-1812.

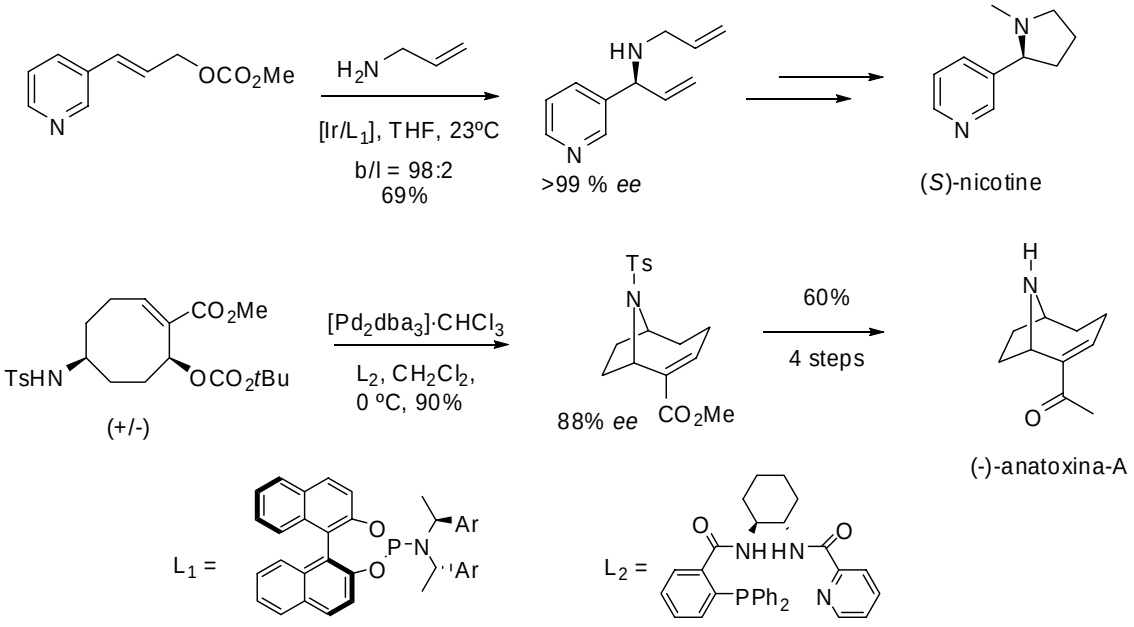
44 Kawatsura, M.; Ata, F.; Wada, S.; Hayase, S.; Uno, H.; Itoh, T. *Chem. Comun*. **2007**, 298-300.

45 Morisaki, Y.; Kondo, T.; Mitsudo, T.-A. *Organometallics* **1999**, *18*, 4742-4746.

46 (a) Plietker, B. *Angew. Chem. Int. Ed*. **2006**, *45*, 1469-1473. (b) Xu, Y.; Zhou, B. *J. Org. Chem*. **1987**, *52*, 974-977.

regioselectivity.[47] Iridium also gives preferently branched products through similar intermediates to that described for Rh with phosphites and phosphorous amidites.[15]

The asymmetric version of allylic alkylation (AAA) has been developed over the past several years.[48] There are two important characteristics that distinguish asymmetric allylic alkylations from essentially all other methods of asymmetric induction. First, the number of mechanisms for enantiodiscrimination, and second, the diversity of bonds types that can be formed. Of the various transition metals used, palladium has been the most extensively applied in a variety of total syntheses. Two representative examples that illustrate the relevance of this reaction are shown in Scheme 16.[49]



Scheme 16

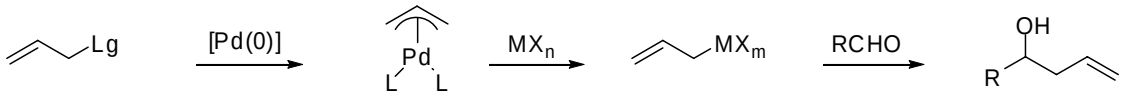
47 Karlström, A. S. E.; Bäckvall, J.-E. in *Modern Organocopper Chemistry*, ed.; Krause, N.; Wieley-VCH: Weinheim, **2001**, p. 259.

48 (a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev*. **1996**, *96*, 395-422. (b) Trost, B. M.; Lee, C. B. in *Catalytic Asymmetric Synthesis II*, ed.; Ojima, I.; Wieley-VCH: Weinheim, **2000**, pp. 593-650. (c) Hayashi, T. in *Catalytic Asymmetric Synthesis*, ed.; Ojima, I.; Wieley-VCH: Weinheim, **2000**, p. 193. (d) Pfaltz, A.; Lautens, M. *Comprehensive Asymmetric Catal*. **1999**, *2*, 833-884.

49 (a) Welter, C.; Moreno, R. M.; Streiff, S.; Helmchen, G. *Org. Biomol. Chem*. **2005**, *3*, 3266-3268. (b) Trost, B. M.; Oslob, J. D. *J. Am. Chem. Soc*. **1999**, *121*, 3057-3064.

1.1.2. Electrophilic allylic substitution

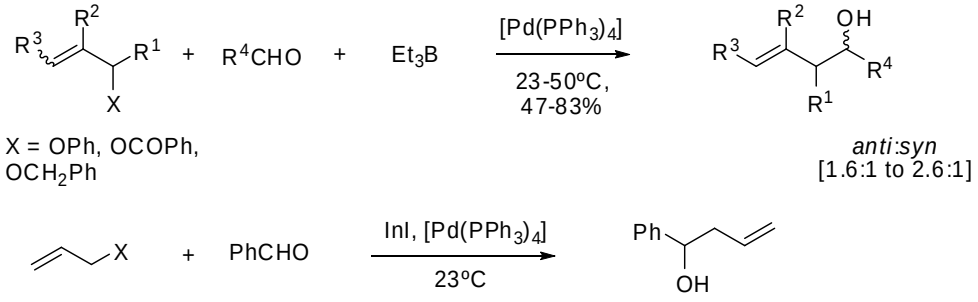
Palladium catalyzed allylations of electrophilic reagents have recently been the subject of great interest due to their wide scope, practical simplicity, and potential for regio- and stereoselective synthesis.[50] In many of these reactions organopalladium compounds derived from halides or esters undergo transmetalation with organometallic reagents (such as $SnCl_2$, $ZnEt_2$, Et_3B, etc) transforming the electrophilic palladium intermediates into nucleophilic organometallic compounds. These organometallic compounds are formed as transient intermediates and react with an elecrophilic partner *in situ*.



Lg = Cl, OCOR
MX_n = $ZnEt_2$, $SnCl_2$, BEt_3, InI, etc.

Scheme 17

Triethylborane[51] and indium(I) salts[52] promote the palladium-catalyzed allylation of aldehydes with allylic substrates via umpolung of π-allylpalladium reactivity.



Scheme 18

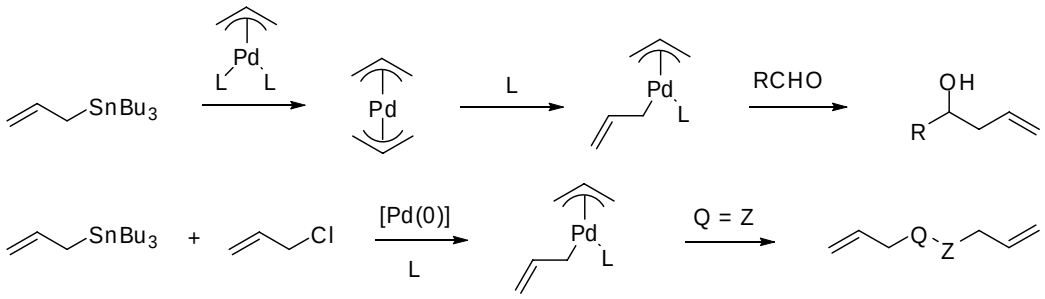
Another approach to perform the umpolung of π-allylpalladium involves the use of allylstannanes and allyl chlorides with catalytic amounts of palladium to form

50 Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163-3185.

51 Kimura, M.; Kiyama, I.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1999**, *40*, 6795-6798.

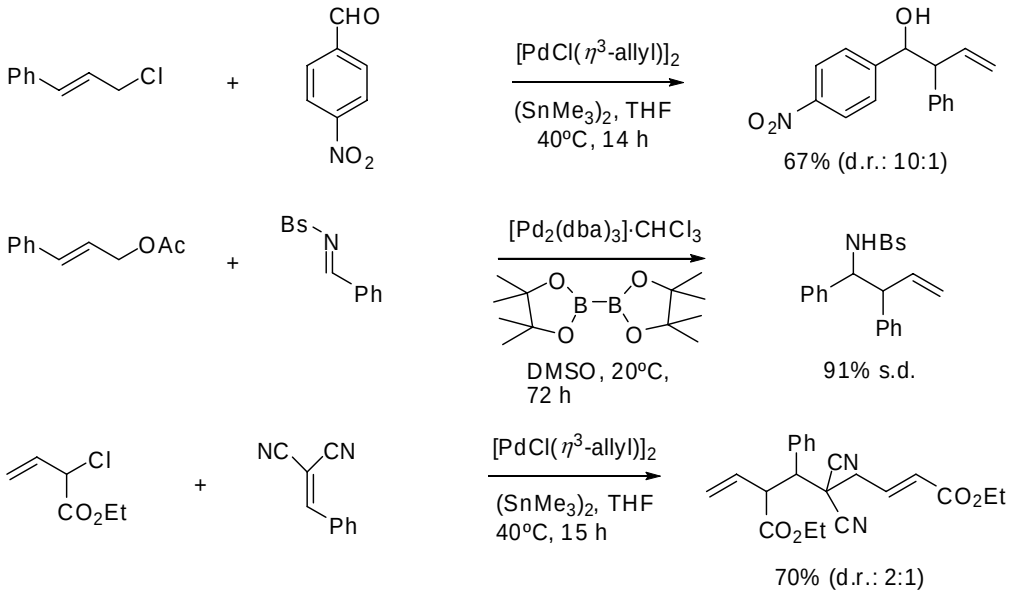
52 Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847-849.

intermediate bisallylpalladium complexes which readily react with electrophiles (Scheme 19). This process will be discussed in more detailed in section 2.1.1.



Scheme 19

Instead of using isolated stannanes, the same process can be carried out from allyl acetates or chlorides in the presence of hexamethylditin[53] or bis(pinacolato)diboron[54] (Scheme 20). The reactions proceed with a remarkably high regioselectivity and in certain cases with high stereoselectivity. In contrast to palladium catalyzed nucleophilic substitution, in this case branched allylic products are obtained. The mechanism for catalytic processes involving the participation of bisallylpalladium complexes will be discussed in section 2.1.1.

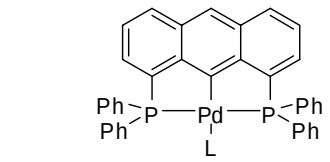


Scheme 20

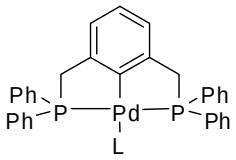
53 (a) Wallner, O. A.; Szabó, K. J. *Org. Lett*. **2002**, *4*, 1563-1566. (b) Wallner, O. A.; Szabó, K. J. *J. Org. Chem*. **2003**, *68*, 2934-2943.

54 Sebelius, A.; Wallner, O. A.; Szabó, K. J. *Org. Lett*. **2003**, *5*, 3065-3068.

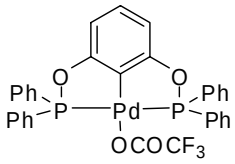
A further innovative development of the palladium catalyzed electrophilic substitution reactions has been achieved by employing monoallyl palladium complexes in which the allyl unit has a nucleophilic character.[55] This type of reactivity occurs when pincer complexes are employed (Scheme 21).



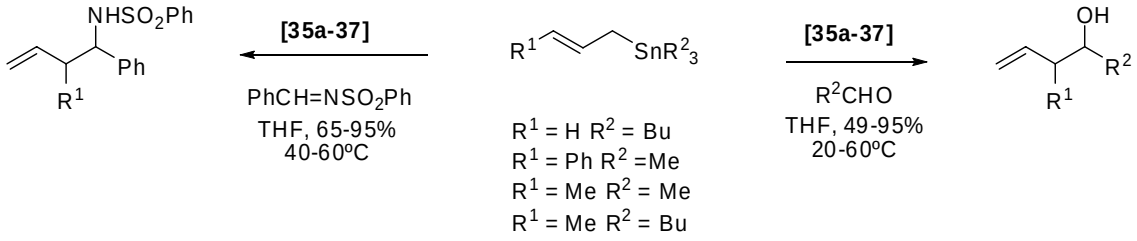
35a L = Cl
35b L = OAc
35c L = BF_4



36a L = Cl
36b L = BF_4



37



Scheme 21

Application of these catalysts eliminates the side reactions that occur in bisallylpalladium catalyzed transformations such as allyl-allyl Stille coupling. Analogues pincer complexes can be used to afford functionalized allylstannanes, allylboronic acids and potassium trifluoro(allyl)borates.[56] The synthesis of these compounds proceeds solely via palladium(II) intermediates without formation of allylpalladium species though.

1.1.3. Intramolecular reactions with alkenes and alkynes

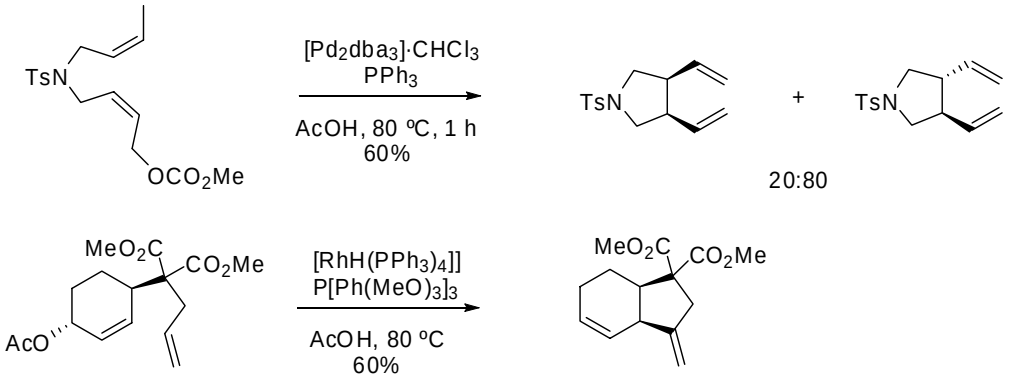
1.1.3.1. The Oppolzer carbocyclization reaction

The Oppolzer carbocyclization reaction consists of the intramolecular insertion of an allyl metal complex into an alkene or an alkyne bond. It is a powerful method for

55 (a) Solin, N.; Kjellgren, J.; Szabó, K. J. *Angew. Chem. Int. Ed*. **2003**, *42*, 3656-3658. (b) Solin, N.; Kjellgren, J.; Szabó, K. J. *J. Am. Chem. Soc*. **2004**, *126*, 7026-7033.

56 (a) Wallner, O. A.; Szabó, K. J. *Org. Lett*. **2004**, *6*, 1829-1831. (b) Sebelius, S.; Olsson, V. J.; Szabó, K. J. *J. Am. Chem. Soc*. **2005**, *127*, 10478-10479. (c) Olsson, V. J.; Sebelius, S.; Selander, N.; Szabó, K. J. *J. Am. Chem. Soc*. **2006**, *128*, 4588-4589.

the construction of five- and six-membered carbo- and heterocycles.[57] The reaction is usually catalyzed by Pd(0) although other metals such as Rh,[58] Ru,[59] Ni[60] or Pt[61] have been employed (some examples are shown bellow).



Scheme 22

This reaction was originally suggested to take place via a pericyclic-type pathway analogous to the lithium and magnesium-ene reactions (Scheme 23, path a). Thus, the allyl electrophile **38** was proposed to react with a Pd(0) complex to form a σ-allylpalladium intermediate, which undergoes a palladium-ene reaction to give **41**. A β-hydride elimination affords either **42** or **43**, depending on the group involved in the elimination of the hydrogen atom.

Another possibility for the step involving the C-C bond formation is outlined in path b (Scheme 23), and involves the η^3-allylpalladium complex **40**. This might take place directly from the electrophile **38** or by associative displacement of two carbons of the allyl moiety by an external ligand.

---

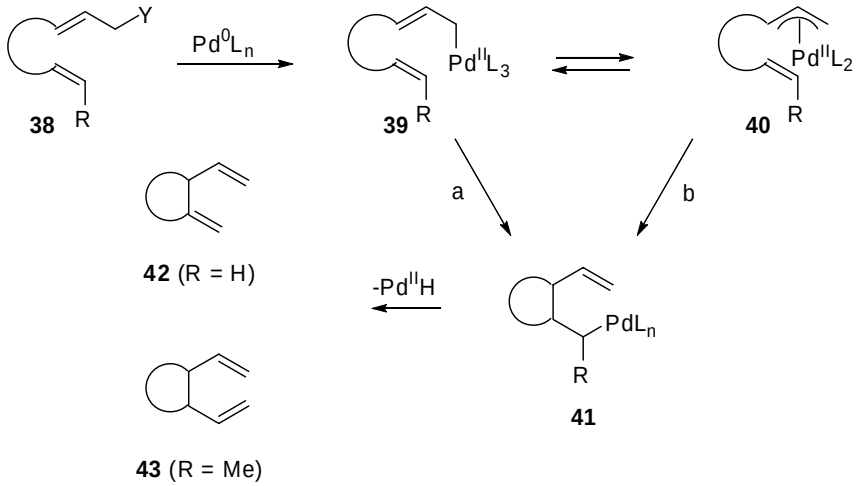
57 Reviews: (a) Oppolzer, W.; Flachsmann, F. *Helv. Chim. Acta* **2001**, *84*, 416-430. (b) Acemoglu, L.; Williams, J. M. in *Handbook of Organopalladiu Chemistry for Organic Synthesis*, ed.; Negishi, E.; Wiley: New York, **2002**; Vol. 1, ch. IV.4, pp. 1845-1886. (c) Oppolzer, W. in *Comprehensive Organic Synthesis*, ed.; Trost, B. M.; Fleming, I; Pergamon: Oxford, **1991**; Vol 5, ch.1.2 (d) Oppolzer, W. in *Comprehensive Organometallic Chemistry II*, eds.: Abel, E. W.; Stone, F. G. A.; Wilkinson, G.; Pergamon: Oxford, 1995, Vol. 12, ch. 8.3. (e) Oppolzer, W. *Pure Appl. Chem*. **1988**, *60*, 39-48. (f) Heumann. A.; Réglier, M. *Tetrahedron*, **1995**, *51*, 975-1015.

58 Oppolzer, W.; Fürstner, A. *Helv. Chim. Acta* **1993**, *76*, 2329-2337.

59 Oppolzer, W.; Fürstner, A.; Ruiz-Montes, J. Umpublished results: mentioned in Oppolzer, W.; Schröder, f.; Kahl, S. *Helv. Chim. Acta* **1997**, *80*, 2047-2057.

60 Oppolzer, W.; Bedoya-Zurita, M.; Zwitzer, C. *Tetrahedron Lett*. **1988**, *29*, 6433-6436.

61 Oppolzer, W. *Angew. Chem. Int. Ed*. **1989**, *28*, 38-52.



Scheme 23

Mechanistic work directed at the determination of the key intermediates of the Oppolzer reaction, carried out by Echavarren et al. suggested that the cylization proceeds through intermediate **40** as related cationic (η^3-allyl)(η^2-alkene) palladium(II) complexes were found to led to the same type of cyclizated products.[62]

The reaction is not very solvent dependent, but a minimum temperature of 60ºC is required for the reaction to proceed. The use of polar protic solvents such as HOAc provides excellent results when the reactions are performed with allylic acetates. If allylic trifluoroacetates are used, the reaction can be performed in non-polar solvents such as toluene.[63] The employment of water soluble phosphines allows the reaction to be carried out in organoaqueous media with Pd(0), Rh(I), and Ni(0) complexes.[64]

Usually, the cyclization leads to the stereoselective formation of *trans* carbocycles. However, the exclusive formation of *cis* derivatives is observed in the presence of Et_2Zn as an additive.[65] In this case, the reaction proceeds through an allylZn

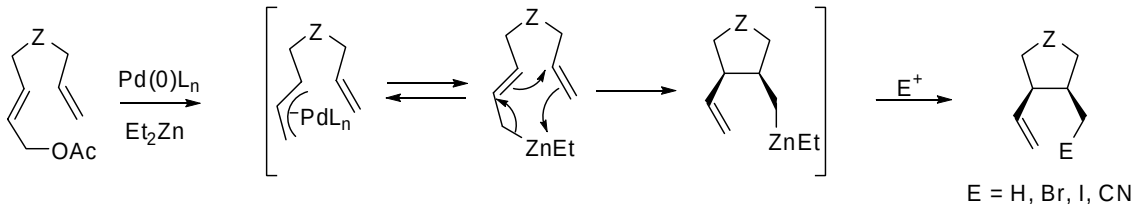
62 (a) Gómez-Bengoa, E.; Cuerva, J. M.; Echavarren, A. M.; Martorell, G. *Angew. Chem. Int. Ed*. **1997**, *36*, 767-769. (b) Cárdenas, D. J.; Echavarren, A. M. *New. J. Chem*. **2004**, *28*, 338-347.

63 (a) Gómez-Bengoa, E. Doctoral Thesis, UAM, **1994**. (b) The use of solvents such us MeCN is posible with subtrates bearing an allylic alcohol: Negishi, E.-I.; Iyer, S.; Rousset, C. *Tetrahedron Lett*. **1989**, *30*, 291-294.

64 Michelet, V.; Galland, J.-C.; Charruault, L.; Savignac, M.; Genêt, J.-P. *Org. Lett*. **2001**, *3*, 2065-2067.

65 (a) Oppolzer, W.; Schröder, F. *Tetrahedron Lett*. **1994**, *35*, 7939-7942. (b) Oppolzer, W.; Flachmann, F. *Tetrahedron Lett*. **1998**, *39*, 5019-5022.

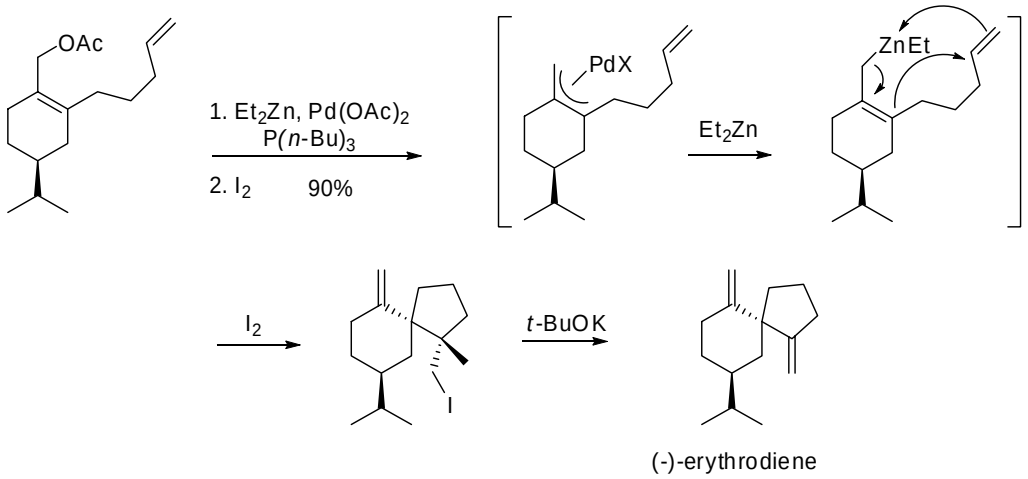
intermediate and it proposed to follow a Zn-ene pathway (Scheme 24). Rhodium and ruthenium also show preferential formation of *cis* derivatives[58,59] (see Scheme 22).



Scheme 24

The σ-alkylPd(II) intermediate (**41**) can be further functionalized by reaction with an organometallic reagent[66] or a molecule of CO.[67,68] In the second case the acyl-Pd(II) complex generated can evolve by solvolysis to give esters or suffer an additional insertion to form new carbocyclic compounds.

An example of application of this methodology in the synthesis of natural products is depicted in Scheme 25. The highly diastereoselective synthesis of (-)-erythrodiene has as a key step a Pd-catalyzed Zn-ene.[65b]



Scheme 25

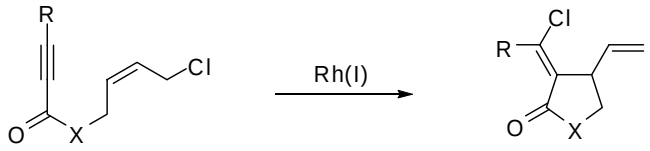
66 (a) Oppolzer, W.; Ruiz-Montes, J. *Helv. Chim. Acta* **1993**, *76*, 1266-1274. (b) Yamada, Y.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett*. **1997**, *38*, 3027-3030.

67 (a) Oppolzer, W.; Keller, T. H.; Bedoya-Zurita, M.; Stone, C. *Tetrahedron Lett*. **1989**, *30*, 5883-5886. (b) Keese, R.; Guidetti-Grept, R.; Herzog, B. *Tetrahedron Lett*. **1992**, *33*, 1207-1210. (c) Ihle, N. C.; Heathcock, C. H. *J. Org. Chem*. **1993**, *58*, 560-563. (d) Terakado, M.; Murai, K.; Miyazawa, M.; Yamamoto, K. *Tetrahedron* **1994**, *50*, 5705-5718.

68 An alternative methodology uses $Ni(CO)_4$ and allyl halides: (a) Solé, D.; Cancho, Y.; Llevaria, A.; Moretó, J. M.; Delgado, A. *J. Org. Chem*. **1996**, *61*, 5895-5904. (b) Villar, J. M.; Delgado, A.; LLevaria, A.; Moretó, J. M.; Maravilles, C. *Tetrahedron* **1996**, *52*, 10525-10546 and references therein.

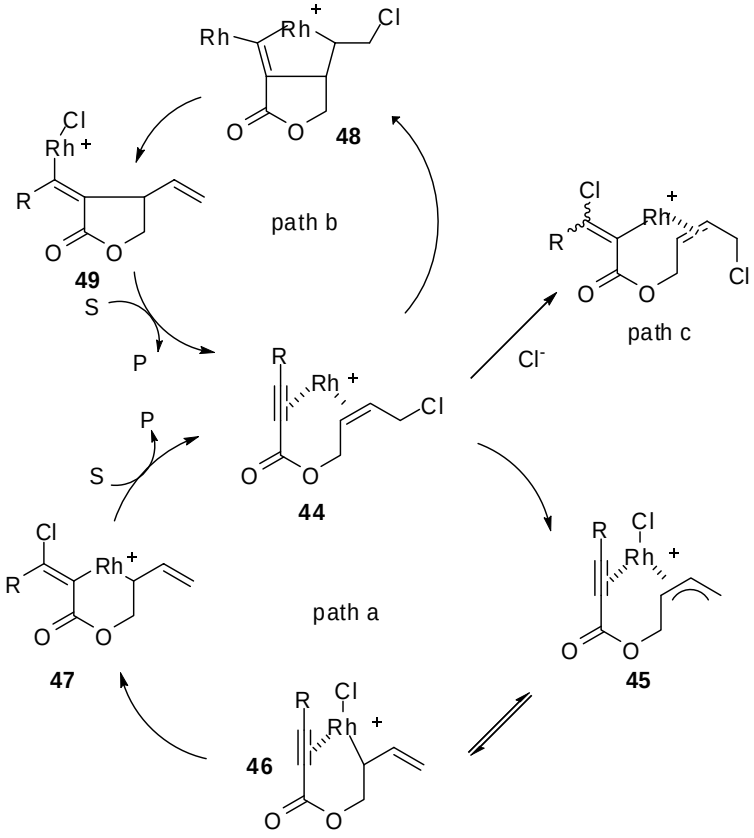
1.1.3.2. Rh(I) catalyzed cyclizations with intramolecular halogen shift

Rh(I) species catalyze the cyclization of 1,6 enynes with an halogen at the allylic position to afford cycloisomerization products where the halogen atom has been transferred from the allyl moiety to the alkyne.[69].



Scheme 26

This reaction is catalyzed by two different Rh(I) systems: $[RhCl(cod)]_2$/dppb/$AgSbF_6$ (cationic system, the ratio Rh:Ag has to be 1:1), and $[RhCl(PPh_3)_3]$ (neutral system). The proposed mechanism for this transformation involves a π-allylrhodium complex as the reaction intermediate (Scheme 27, path a). Two other possible pathways for the reaction to proceed are: oxidative cyclometalion (path b) and chlororhodation (path c). Both have been excluded on the base of some experimental results.



Scheme 27

69 (a) Tong, X.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc*. **2003**, *125*, 6370-6371. (b) Tong, X.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc*. **2004**, *12*, 7601-7607.

The mechanism via a π-allyl rhodium complex is based on a precedent for the oxidative addition of an allyl chloride with $[RhCl(PPh_3)_3]$ to generate a $Rh(PPh_3)_2Cl_2(\pi\text{-}C_3H_5)$ species.[70] If oxidative addition of an allylic halide is faster than the oxidative cyclometalation in path b, an enyne-coordinated Rh-(I) species (**44**) reacts with the allylic chloride to form an π-allyl rhodium complex (**45**). This π-allyl intermediate could convert to **46** via η^3-η^1 isomerization. Addition of the rhodium chloride bond of **46** to the alkyne forms another intermediate (**47**). Reductive elimination of **47** gives the product and regenerates the catalytic Rh(I) species.[71]

Although the mechanism through oxidative cyclometalation (path b) would lead to the correct geometry at the double bond, reductive elimination of the rhodium(alkenyl)chloride (**49**) is rare, and the transformation requires harsh conditions. In general, rhodium(alkenyl)halides will undergo further reactions instead of reductive elimination.[72]

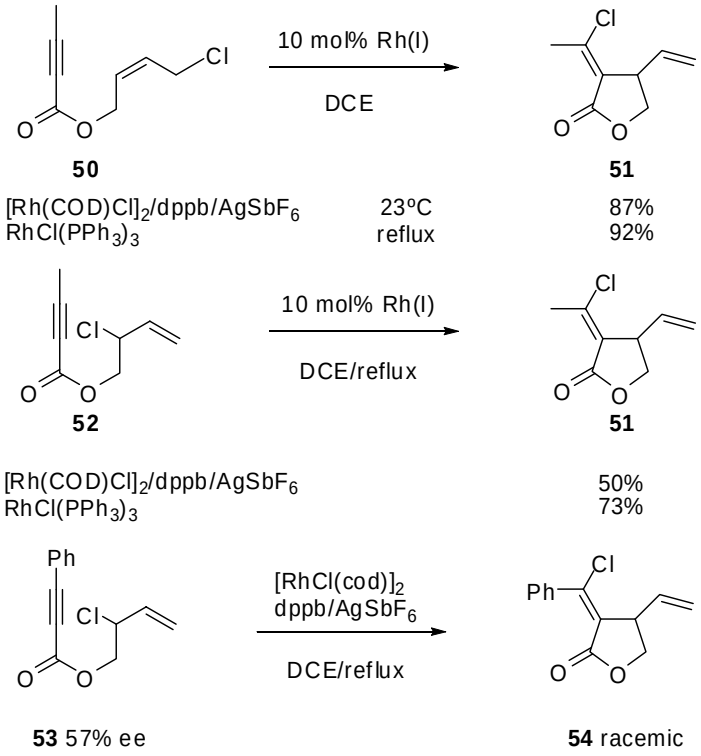
A mechanism involving chlororhodation followed by alkene insertion and β-Cl elimination (path c) was rejected because under the reaction conditions no free chloride ion is present to initiate chlororhodation in the presence of an excess halide scavenger, $AgSbF_6$.

Further evidence to support the mechanistic pathway involving π-allylrhodium intermediates was given by two control experiments outlined in Scheme 28. First, compound **50** and its regioisomer **52** were converted to the same product **51** in good yields. This result show that these two products react through a common intermediate. Second, chiral substrate **53** was transformed to the racemic product **54**, which is possible by isomerization of the resulting π-allylrhodium(III) intermediate.

70 (a) Lawson, D. N.; Osborn, J. A.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1733-1736. (b) Volger, H. C.; Vrieze, K. *J. Organomet. Chem*. **1967**, 527-536.

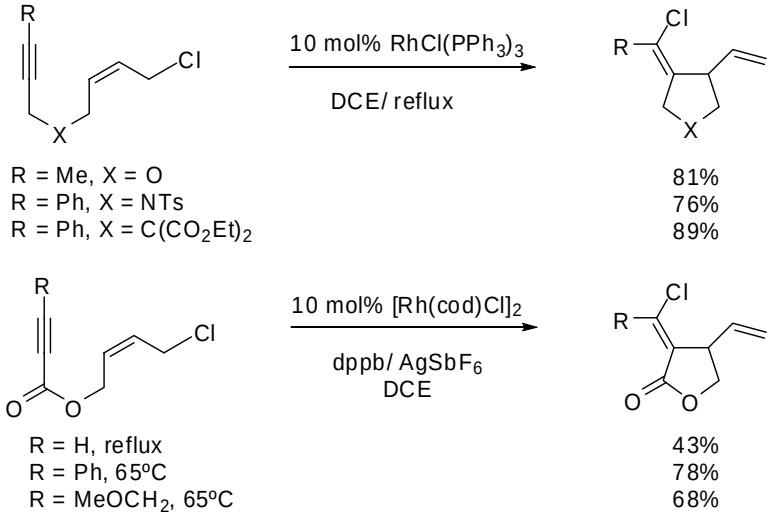
71 Sato, Y.; Oonishi, Y.; Mori, M. *Angew. Chem. Int. Ed*. **2002**, *41*, 1218-1221.

72 Amii, H.; Kishikawa, Y.; Uneyama, K. *Org. Lett*. **2001**, *3*, 1109-1112.



Scheme 28

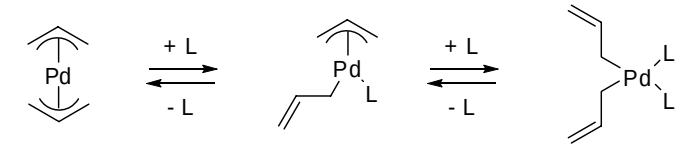
$[RhCl(PPh_3)_3]$ gives in general a better yield in the cyclization than $[RhCl(cod)_2]_2$ except for terminal alkynes. Examples of the scope of this reaction are shown in Scheme 29.



Scheme 29

2. Bis(π-allyl)complexes

Bisallylpalladium intermediates can be classified as catalytic amphiphilic (i.e., both electrophilic and nucleophilic) species,[73] which are exceptionally useful reagents in organic synthesis. In a bisallylpalladium complex, the allyl ligands can coordinate to the central atom with different hapticity (Scheme 30).

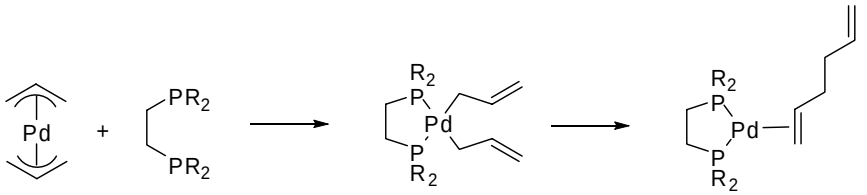


55a (η^3,η^3) **55b** (η^1,η^3) **55c** (η^1,η^1)

Scheme 30

The η^3,η^3-coordination mode **55a**, may have two different configurations depending on the orientation of the allyl ligands. According to NMR results, the dominating species in solution is the form in which the allyl ligands are *trans*, however the *cis*-form can also be detected, because of the small energy difference.[74]

Coordinating ligands (L, Scheme 30) react with η^3,η^3 complexes leading to the η^3,η^1-bisallylpalladium species **55b**, which are the presumed substrates of the electrophilic attack.[74,75] The formation of the η^1,η^1-bisallylic isomer **55c**, is promoted in the presence of excessive amounts of strongly coordinating ligands. This has been observed with various bidentate phosphines. Complexes of type **56**, can spontaneously undergo reductive elimination to form complexes **57** (Scheme 31).[76]



56 **57**

Scheme 31

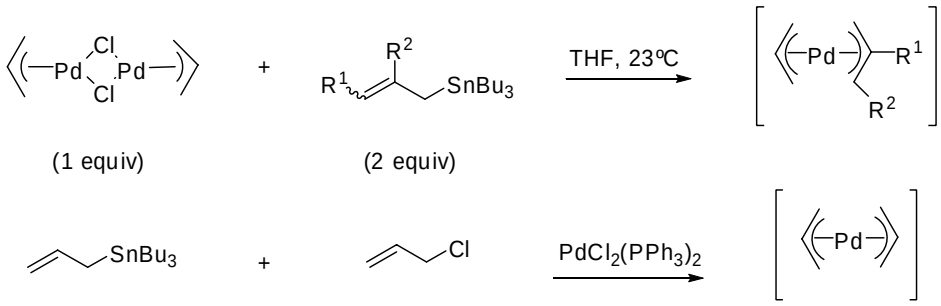
73 Nakamura, H.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc*. **1997**, *119*, 8113-8114.

74 Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc*. **1996**, *118*, 6641-6647.

75 Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, B.; Schenker, G.; Schick, K.-P.; Schroth, G. *Organometallics* **1985**, *4*, 1945-1953.

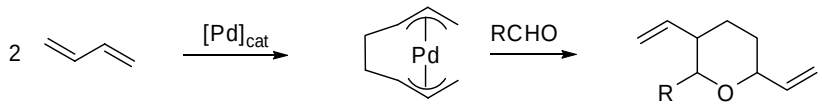
76 Krause, J.; Bonrath, W.; Porschke, K. R. *Organometallics* **1992**, *11*, 1158-1167.

Bisallylpalladium intermediates can be formed in a number of catalytic reactions. Yamamoto and co-workers have generated bisallylpalldium intermediate **55a** from allyltributylstannane and palladium complexes (Scheme 32).[74] The bisallylpalladium intermediate has also been formed from a mixture of allyltributylstannane and allylchloride in the presence of a palladium complex.[73]



Scheme 32

In catalytic processes of great industrial importance, such as the dimerization and telomerization of conjugated dienes, reactive bisallylpalladium intermediates are also formed. Tsuji and co-workers have shown that treatment of butadiene with aldehydes leads to the formation of 3,6-divinyltetrahydropyranes (Scheme 33).[77] This reaction is supposed to proceed through a bisallylpalladium intermediate **58a** by employing the amphiphilic reactivity of this complex.

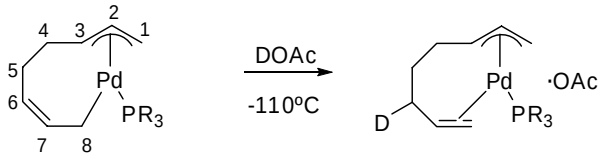


58a

Scheme 33

Jolly and co-workers studied the mechanism of the palladium-catalyzed dimerization of butadienes in the presence of phosphine ligands.[75] Under the conditions applied, the (η^3,η^3-octadienyl)palladium complex **59a** could not be detected, but formation of the η^1,η^3-allyl form **59b** could be observed at low temperature (-30ºC). The authors also studied the reactivity and regiochemistry of the elecrophilic attack on **59b**. It was found that complex **59b** can be protonated by a weak acid, at -110ºC. Furthermore, by using DOAc, it was established that the protonation takes place exclusively at the C6 position (Scheme 34).

77 Ohno, K.; Mitsuyasu, R.; Tsuji, J. *Tetrahedron* **1972**, *28*, 3705-3720.



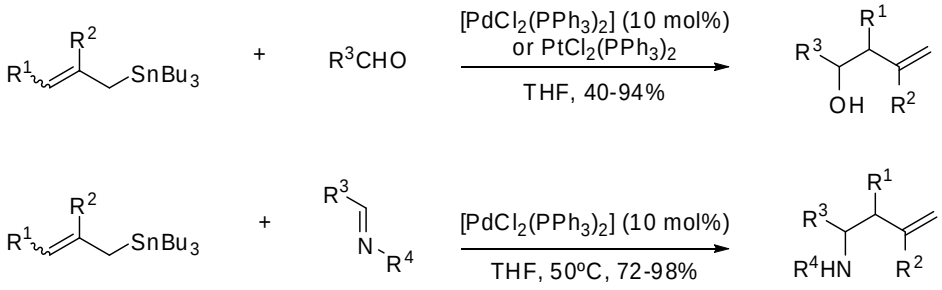
59b

Scheme 34

2.1. Allylation reactions via bis(η^3-allyl)complexes

2.1.1. Allylation of aldehydes and imines

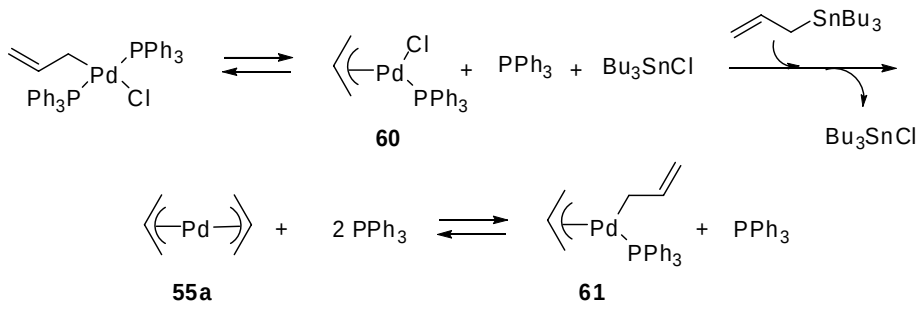
Bis(η^3-allyl)complexes were found to be the active species in the catalyzed allylation of aldehydes and imines with allyltrialkylstannanes. The reaction took place in the presence of Pd(II) or Pt(II) complexes to give homoallylic alcohols and amines under essentially neutral conditions with good yields and selectivity (Scheme 35).[74]



Scheme 35

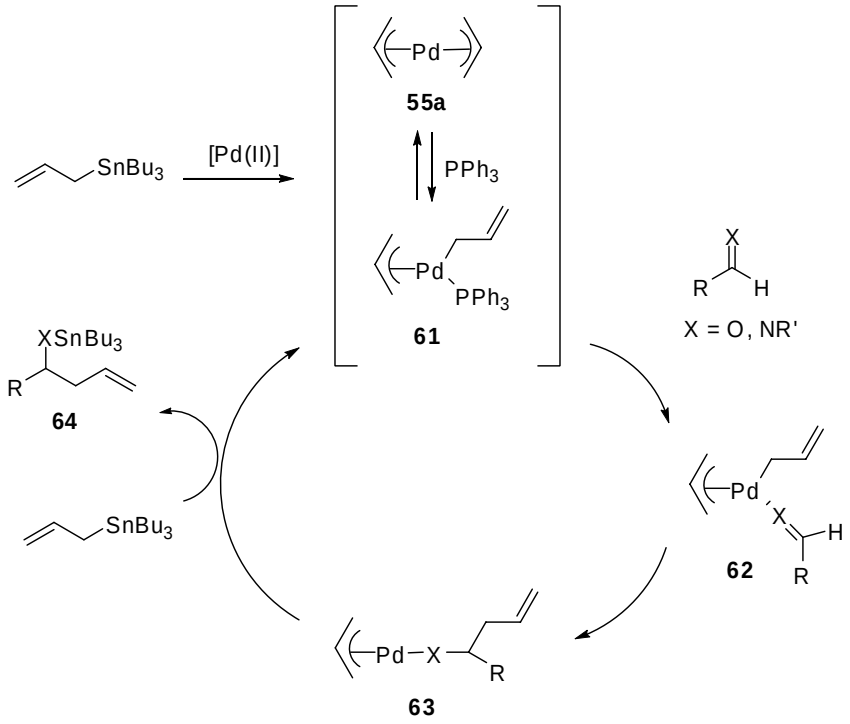
Although aldehydes are usually more reactive than imines toward organometallics reagents, in this particular case the reaction with imines was faster and gave better yields. Thus, imines could be chemoselective allylated in the presence of aldehydes.

That bis(η^3-allyl)complexes were the active catalytic species in these reactions was determined by mixing π-allylpalladium chloride **60**, with PPh_3 and Bu_3SnCl. This mixture did not react with benzaldehyde. However, after the addition of allyltributyltin to this mixture, the allylation took place immediately. Under these conditions the formation of bis(η^3-allyl)palladium **55a** was observed by NMR (Scheme 36).[74]



Scheme 36

The proposed catalytic cycle is depicted below (Scheme 37).[74]

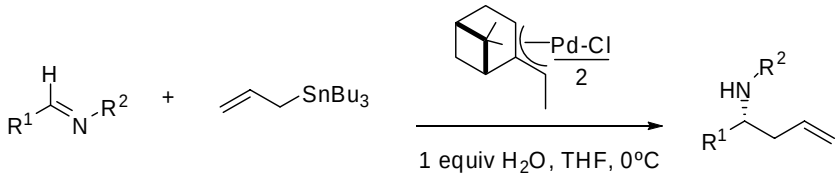


Scheme 37

Complex **61** is generated *in situ* by the reaction of 2 equiv of allyltributylstannane and $[PdCl_2(PPh_3)_2]$. The coordination of the aldehyde or imine to **61** led to a π-allyl-σ-allyl palladium complex **62**. Subsequent electrophilic attack of the coordinated aldehyde or imine would produce the homoallyloxystannane derivative **63**. Transmetalation of **63** with allyltritutylstannane led to the corresponding homoallyl derivative **64**.

The reaction could be conducted in the absence of phosphine ligands but required stoichiometric amounts of palladium complex **55a**. In this case direct formation of complex **62** occurred from electrophilic attack of the aldehyde or imine to **55a**.

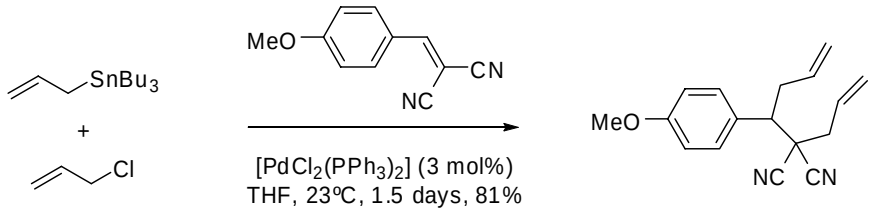
With the proper choice of the two allyl ligands of the bis(η^3-allyl)complex, catalytic asymmetric allylation was also possible. By this way diverse chiral homoallylamines were synthesized with good to high yields (42-87%) and moderate to high enantioselectivities (55-90 *ee*).[78]



Scheme 38

2.1.2. Bis-allylation reactions

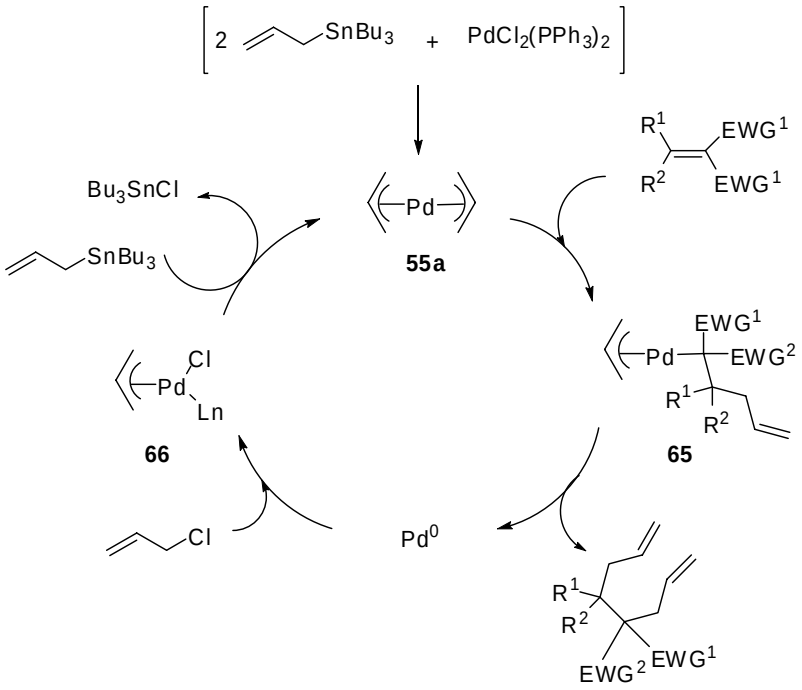
Due to the amphiphilic character of bis(η^3-allyl)allylpalladium complexes they can undergo an initial electrophilic attack on one of the allyl moieties, followed by a nucleophilic attack on the other. Substrates bearing both nucleophilic and electrophilic carbons react with bis(η^3-allyl)allylpalladium complexes to give bis-allylated compounds. Yamamoto and co-workers described that trisubstituted activated olefins underwent the double allylation process to give 1,7-octadienes in high yields.[73]



Scheme 39

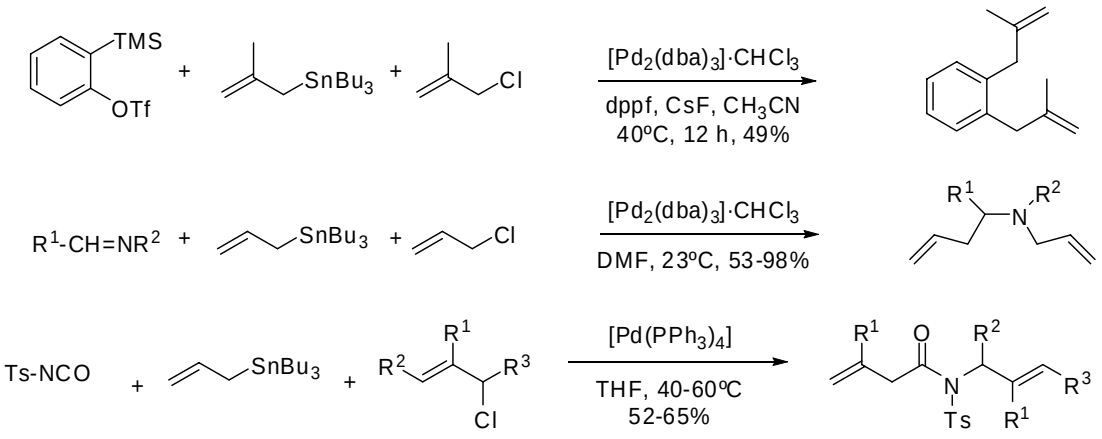
A reasonable mechanism for this transformation was proposed by the formation of the bis(η^3-allyl)allylpalladium intermediate **55a**, which reacts as a nucleophile with the electron deficient carbon of the Michael acceptor to give the alkyl-allylPd complex **65**. Subsequent reductive coupling from **65** led to the corresponding 1,7-octadienes together with Pd(0) species. At this stage, the π-allyl group of **65** could react with the nucleophilic carbon center. The oxidative insertion of Pd(0) into allyl chloride would produce the π-allylpalladium chloride complex **66** (Scheme 40).

78 Fernández, R. A.; Stimac, A.; Yamamoto, Y. *J. Am. Chem. Soc*. **2003**, *125*, 14133-14139.



Scheme 40

Similar processes using benzynes,[79] imines,[80] and isocyanates[81] have also been described (Scheme 41).



Scheme 41

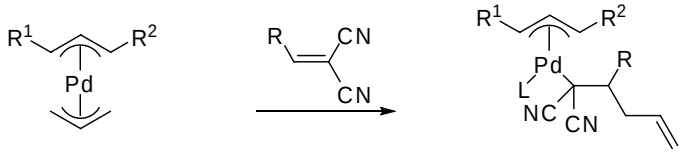
When both the allyl chloride and the allylstannane components have a different substituent pattern, a mixture of isomeric products can be obtained. Experimental and theoretical studies showed that the regioselectivity of the reaction can be controlled by

79 Yoshikawa, E.; Radhakrishman, R. V.; Yamamoto, Y. *Tetrahedron Lett*. **2000**, *41*, 729-731.

80 Nakamura, H.; Aoyagi, K.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc*. **2001**, *123*, 372-377.

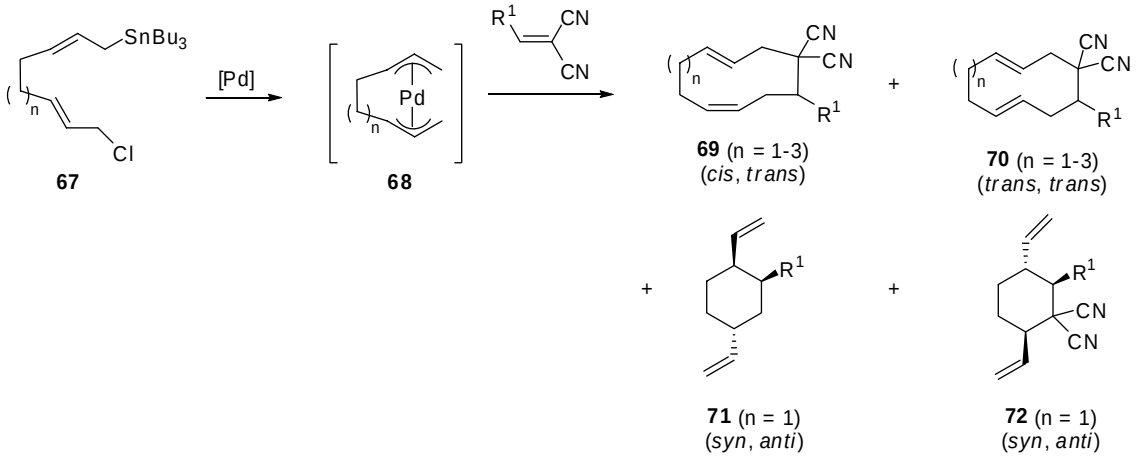
81 Solin, N.; Narayan, S.; Szabó, K. J. *Org. Lett*. **2001**, *3*, 909-912.

choosing the appropriate substitution pattern.[82] The electrophilic attack on an unsymmetrically substituted bis(η^3-allyl)allylpalladium complex takes place at the unsubstituted allyl moiety (Scheme 42). The regioselectivity of the subsequent nucleophilic attack might also be controlled by the steric bulk of the ligand.[83] Therefore, in order to achieve high degrees of regioselectivity, the reaction should be performed between a terminally substituted allyl partner and an unsubstituted one.



Scheme 42

The intramolecular version of the bisallylation enables the synthesis of 6- 10- and 11-membered carbocycles.[80] The required carbon tethered bis(η^3-allyl)palladium complexes (**68**) can be generated *in situ* from compounds of type **67** bearing both an allylstannane and allyl chloride functionalities.



Scheme 43

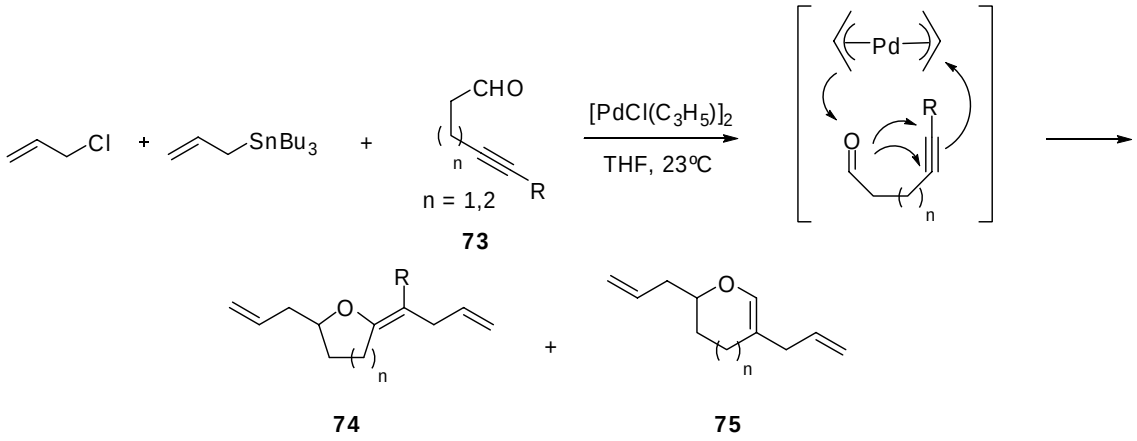
For n = 1 two types of products can be obtained: products arising from a formal [4+2] cycloaddtion (*exo-exo* mode) and products arising from a [8+2] cycloaddition (*endo-endo* mode). The selectivity of the reaction depends on the nature of the solvent. Thus, in polar coordinating solvents such as DMF or THF, the [4 +2] adducts (**69**, **70**) were obtained predominantly, whereas in non coordinating solvents such as CH_2Cl_2 the [8 + 2] adducts (**71**, **72**) were produced in significant amounts. The latter became the

82 Solin, N.; Narayan, S.; Szabó, K. J. *J. Org. Chem*. **2001**, *66*, 1686-1693.

83 Keinan, E.; Shai, M. *Chem. Commun*. **1984**, 648-650.

major products in the reaction with olefins bearing a phenyl group with an electron-withdrawing substituent at the *para* position. By increasing the size of the tether, the formation of macrocicles (*endo*-*endo* mode cycloaddition) was favored.

Bis(η^3-allyl)allylpalladium complexes have also been used for the synthesis of cyclic ethers[84] and 1,2-dihydroisoquinolines.[85] Cyclic ethers were obtained by a nucleophilic allylation of alkynylaldheydes **73** followed by the alkoxyallylation of the alkyne bond in a tandem manner to produce the corresponding *exo*- and *endo*-cyclic ethers **74** and or **75**.



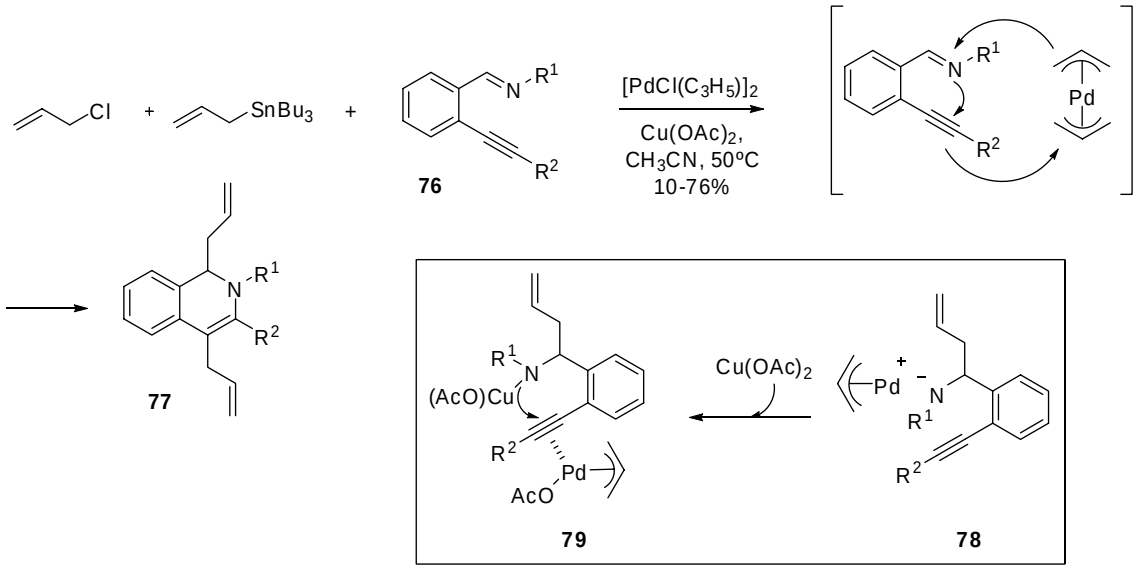
Scheme 44

The selectivity of 5-*exo* and 6-*endo* cyclizations was dependent on the functional groups present on the acetylenes. The alkynylaldehydes having an electron-withdrawing group gave the 5-*exo* products exclusively or very predominantly (51-86%), while those having an electron-donating group at the R position afforded the 6-*endo* products predominantly (37-59%).

The construction of 1,2-dihydroisoquinolines **77** was carried out by a Pd(II)-$Cu(OAc)_2$ cocatalyzed tandem bisallylation of the imine-alkyne functional groups of the *ortho*-alkynyl-arylimines **76**. $Cu(OAc)_2$ was proposed to assist the cleavage of the Pd-N interaction in intermediate **78** and the formation of the Pd-alkyne complex **79**.

84 Nakamura, H.; Ohtaka, M.; Yamamoto, Y. *Tetrahedron Lett*. **2002**, *43*, 7631-7633.

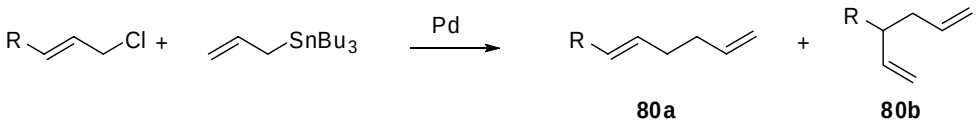
85 Ohtaka, M.; Nakamura, H.; Yamamoto, Y. *Tetrahedron Lett*. **2004**, *45*, 7339-7341.



Scheme 45

2.2. Allyl-allyl coupling reactions

The Stille cross-coupling reaction between allylstannanes and allyl carboxylates[86,87] or allyl bromides[88,89] allows the synthesis of 1,5-hexadiene coupling products **80a** and **80b** in moderate to high yields (Scheme 46).[90]



Scheme 46

86 (a) Trost, B. M.; Keinan, E. *Tetrahedron Lett*. **1980**, *21*, 2595-2598. (b) Keinan, E.; Peretz, M. *J. Org. Chem*. **1983**, *48*, 5302-5309.

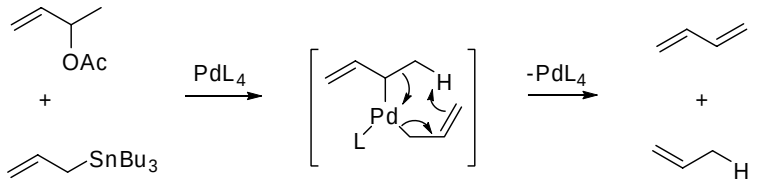
87 Allyl phosphates also couple with stannanes: Kosugi, M.; Ohashi, K.; Akuzawa, K.; Nazazoe, T.; Sano, H.; Migia, T. *Chem. Lett*. **1987**, 1237-1238.

88 Godschalx, J.; Stille, J. K. *Tetrahedron Lett*. **1980**, *21*, 2599-2602.

89 For the palladium-catalyzed carboxylative coupling of allylstannanes with allyl chlorides, see: Franks, R. J.; Nicholes, K. M. *Organometallics* **2000**, *19*, 1458-1460.

90 (a) Stille, J. K. *Angew. Chem. Int. Ed*. **1986**, *25*, 508-524. (b) Mitchell, T. N. *Synthesis* **1992**, 803-815. (c) Farina, V.; Roth, G. P. *Adv. Met. Org. Chem*. **1996**, *5*, 1-53. (d) Farina, V.; Krishnamurthy, V.; Sctott, W. J. *Org. React*. **1997**, *50*, 1-652.

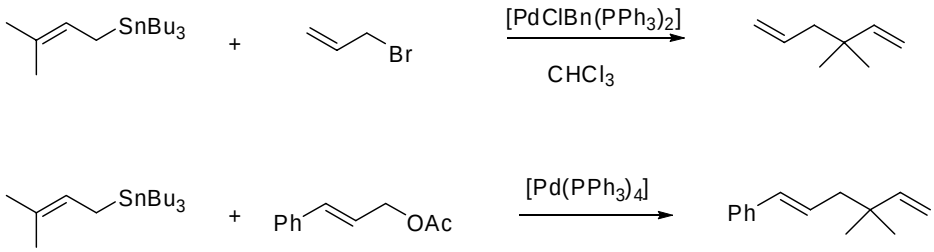
In this process β-hydrogen elimination competes with the C-C coupling reaction. It has been proposed that the β-H elimination proceeds through intermediates of type **81** by a concerted pathway, probably via a 6-electron/6-center transition state (Scheme 47).[91]



81

Scheme 47

Because of the clean allylic inversion observed on the nucleophilic compound (Scheme 48), initially a direct attack of the stannane on a (η^3-allyl)palladium complex was proposed as the most likely reaction pathway.



Scheme 48

Later it has been established that a bis(η^3-allyl)palladium is formed[92] after transmetalation of the initial (η^3-allyl)palladium complex with the allyltin. Bis(η^3-allyl)palladium does not have any tendency to undergo reductive elimination,[93,94] and in the presence of phosphine ligands generates a η^1,η^3-complex. Theoretical calculations showed that the most favourable pathway for the reaction involves a reductive elimination from a bis(η^1-allyl)palladium complex[95] generated by coordination of a second phosphine ligands (Scheme 49). Interestingly, in the reductive elimination step

91 Keinan, S.; Kumar, S.; Dangur, V.; Vaya, J. *J. Am. Chem. Soc*. **1994**, *116*, 11151-11152.

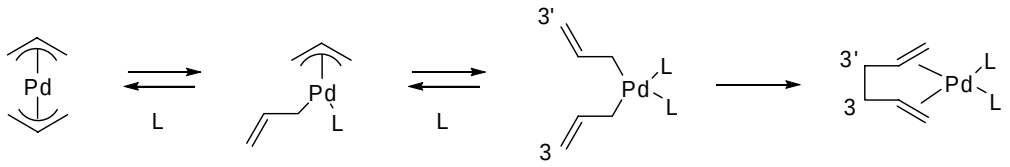
92 Nakamura, H.; Bao, M.; Yamamoto, Y. *Angew. Chem. Int. Ed*. **2001**, *40*, 3208-3210.

93 Nakamura, H.; Aoyagi, K.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc*. **2001**, *123*, 372-377.

94 Szabó, K. J. *Chem. Eur. J*. **2000**, *6*, 4413-4421.

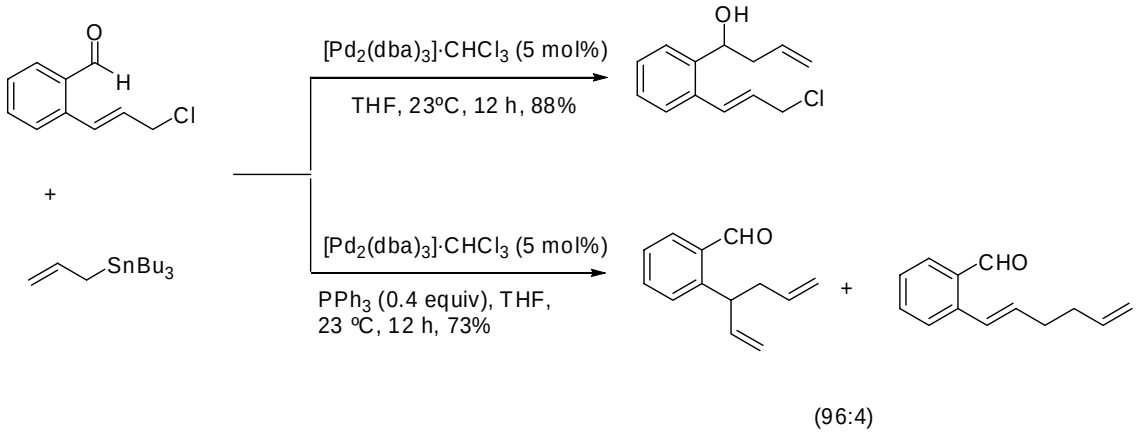
95 Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J*. **2002**, *8*, 3620-3628.

the formation of a C3-C3' bond is favoured significantly over the formation of a C1-C1' or a C1-C3' bond.



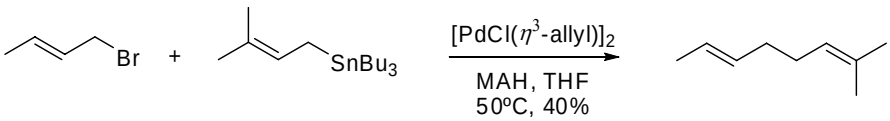
Scheme 49

The presence or absence of phosphines played a crucial role in determining the reactivity of the stannane moiety towards the coupling with allyl chlorides or the allylation of aldehydes.[92] When substrates containing an allyl chloride unit and an aldehyde group in the same molecule were treated with allyltributyltin, the products arising from the Stille coupling were observed only in the presence of phosphines (Scheme 50). On the other hand, in the absence of phosphines, the allylation of the aldehydes occurs.



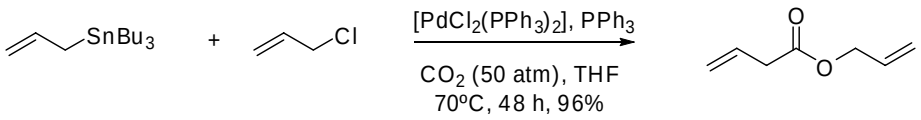
Scheme 50

Although the presence of phosphines is essential for the coupling to proceeds with good yields, a catalytic process in the absence of phosphines has also been developed. In this case, substoichiometric amounts of maleic anhydride were needed. The selectivity of the process was opposite to the one obtained in the presence of phosphines (Scheme 51).



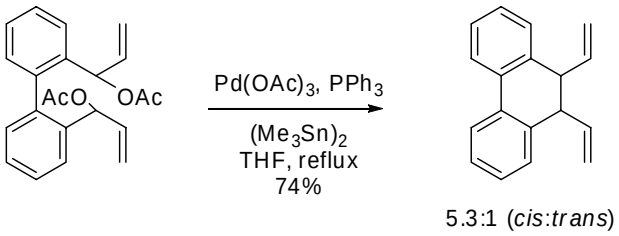
Scheme 51

When CO_2 was included in the cross-coupling reaction, esters were obtained.[89] The reaction is specific for allylic substrates and quite sensitive to the steric/electronic character of the substrates. The use of unsymmetrical allylchlorides and allyllstannanes led to a statistical mixture of all possible esters.



Scheme 52

A modified version of the coupling reaction of allyl acetates and allylstannanes consists of the Pd(0) catalyzed reductive coupling of allyl acetates in the presence of hexamethyldistannane.[96] In this transformation, the allylstannane is presumably generated *in situ* in a Pd catalyzed process.[97] The reaction has been performed both in inter- and intramolecular fashions and, once more, the external attack of the stannane onto a (η^3-allyl)Pd intermediate has been proposed as the most probable reaction pathway (Scheme 53).[98]



Scheme 53

The use of allylic silanes as nucleophiles in the Pd catalyzed allyl-allyl coupling reactions is more scarce.[99] Only a few examples can be found in the literature and the proposed reaction mechanism involves external attack of the silane to the (η^3-allyl)Pd complex, as in the case of their tin counterparts.

Lewis acids can also promote allyl coupling of allylsilanes and allylstannanes leading to 1,5-dienes but stoichiometric amounts of the Lewis acid are required. Only

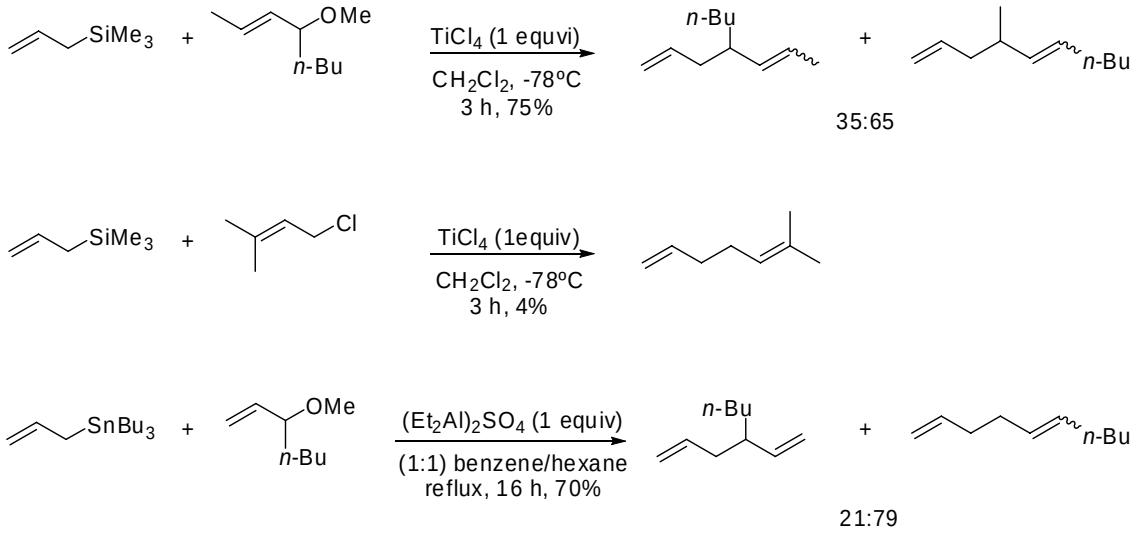
96 Reductive coupling between aryl bromides and allylacetates: (a) Trost, B. M.; Walchli, R. *J. Am. Chem. Soc.* **1987**, *109,* 3487-3488. (b) Yokohama, Y.; Ito, S.; Takahashi, Y.; Murakami, Y. *Tetrahedron Lett.* **1985**, *26*, 6457-6460.

97 Yoshida, J.; Funahashi, H.; Iwasaki, H.; Kawabata, N. *Tetrahedron Lett.* **1986**, *27*, 4469-4472.

98 Trost, B. M.; Pietrusiewicz, K. M. *Tetrahedron Lett.* **1985**, *26*, 4039-4042.

99 (a) Hatanaka, Y.; Hiyama T. *J. Org. Chem.* **1988**, *53,* 918-920. (b) Hatanaka, Y.; Ebina, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1991**, *113,* 7075-7076.

cross-coupled products with regioselective transposition in the allylic part of the allylmetallics are obtained. The regioc hemistry with respect to the allylic electrophiles depends on the stereoelectronic character of the allylic substrates (Scheme 54).[100]



Scheme 54

The role of the Lewis acid is to activate the allyl electrophile toward the nucleophilic attack by coordination. In the case of allylsilanes, $TiCl_4$ was needed to perform the coupling, while in the case of more reactive allylstannanes, a weak Lewis acid such as boron trifluoride etherate or bis(diethylaluminum)sulphate was sufficient.

2.3. Synthesis of carbocycles via bis(η^3-allyl)complexes

The synthesis of the lobane diterpenes, such as fuscol (**82**) and lobatriene (**83**), is of interest as this group of marine natural products displays potent anti-inflammatory activity through selective blocking of the synthesis of leucotrienes.[101] Interestingly, lobane diterpenes posses the opposite configurations at the three stereogenic centers of the six-membered ring to those displayed by the elemane sequiterpenes, such as β-elemene (**84**)[102] and elemol (**85**) (Figure 4). These terpenes posses *trans*-1,2-dialkenyl

100 Hosomi, A.; Imai, T.; Endo, M.; Sakurai, H. *J. Organomet. Chem*. **1985**, *285*, 95-107.

101 (a) Gopichand, Y.; Schmitz, F. J. *Tetrahedron Lett*. **1978**, 3641-3644. (b) Shin, J.; Fenical, W. *J. Org. Chem*. **1991**, *56*, 3153-3158. (c) Chai, M.-C.; Wang, S.-K.; Dai, C.-F.; Duh, C.-Y. *J. Nat. Prod*. **2000**, *63*, 843-844, and references therein.

102 (a) Patil, L. J.; Rao, A. S. *Tetrahedron Lett*. **1967**, *8*, 2273-2172. (b) McMurry, J. E.; Kocovski, P. *Tetrahedron Lett*. **1985**, *26*, 2171. (c) Wakamatsu, T.; Hara, H.; Taira, K. *Heterocycles* **1987**, *26*, 1203-1206.

groups. However, epi-elemol (**86**)[103] a rare member of the elemane family of sesquiterpenes, bears *cis*-1,2-dialkenyl groups.

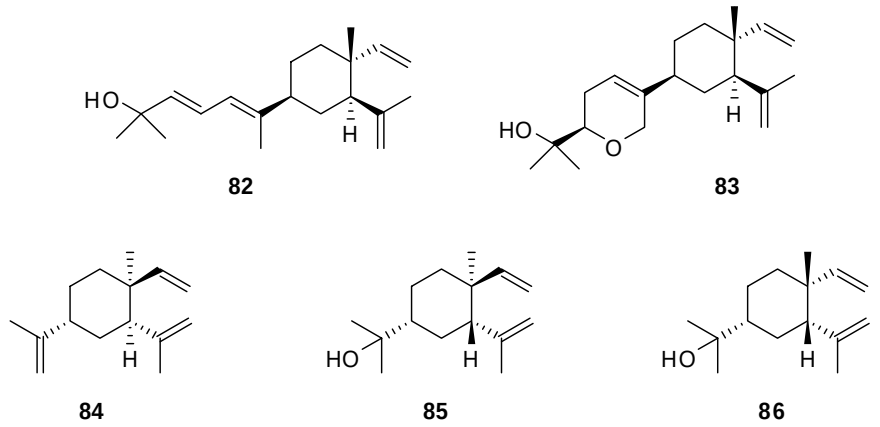
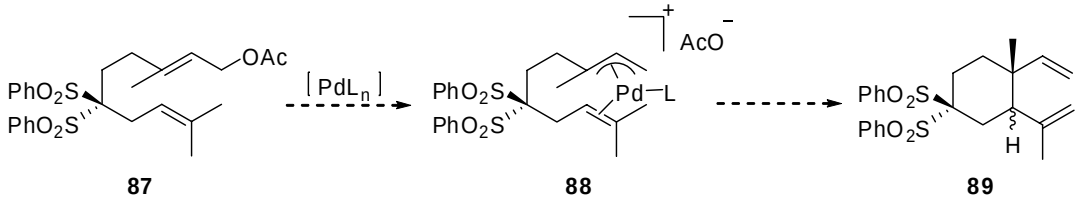


Figure 4

In our research group two different approaches towards the synthesis of this family of natural products have been made. First, the construction of the six-membered rings of the elemanes was envisaged through an Oppolzer carbocyclization of substrate **87**, via a (η^2-alkenyl)(η^3-allyl)palladium complexes of type **88** (Scheme 55).



Scheme 55

Although formation of six-membered carbocycles using the Oppolzer cyclization was possible with monosubstituted alkenes,[104] substrate **87** with methyl groups at C-3 of the allyl and at the olefin, failed to cyclize with palladium catalysts under all the conditions examined.[105]

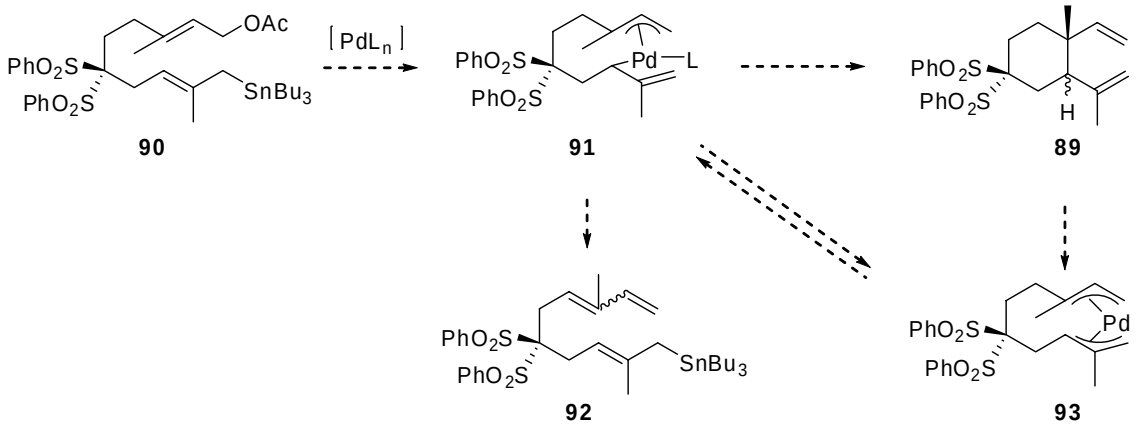
A different synthetic strategy was conceived based on the use of an intramolecular palladium catalyzed cross-coupling of an allyl stannnane with an allyl acetate **90**. This coupling reaction would proceed through complexes of type **91**, or its

103 Thomas, A. F.; Ozainne, M. *Helv. Chim. Acta*. **1978**, *61*, 2874-2880.

104 Gómez-Bengoa, E.; Noheda, P.; Echavarren, A. M. *Tetrahedron Lett*. **1994**, *35*, 7097-7098.

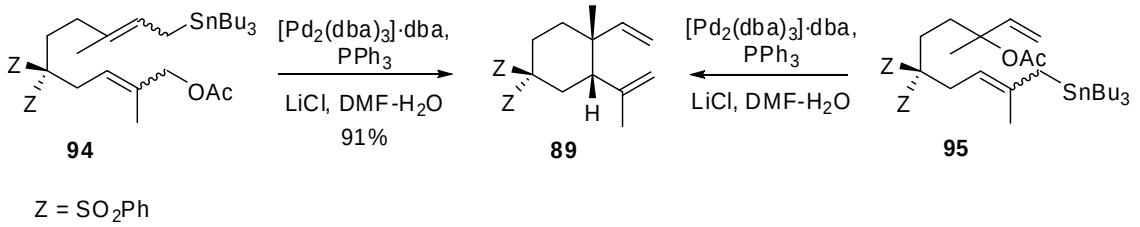
105 Gómez-Bengoa, E. *Doctoral Thesis*, UAM, **1994**.

regioisomer, which would undergo reductive elimination to give carbocycle **89**. Alternatively, a bis(η^1-allyl)palladium complex or a bis(η^3-allyl)palladium complex **93** might be the precursor of **89**.[106]



Scheme 56

Despite the non particularly encouraging precedents for allyl-allyl couplings, which established that these reactions are in general limited to substrates which are not prone to undergo β-hydrogen elimination, the intramolecular coupling could be efficiently carried out from substrate **94** without any significant elimination. This was done using a catalyst prepared from $[Pd_2dba_3]\cdot dba$ and PPh_3 (2 equiv per Pd) in the presence of LiCl in 0.5 % aqueous DMF (Scheme 57).



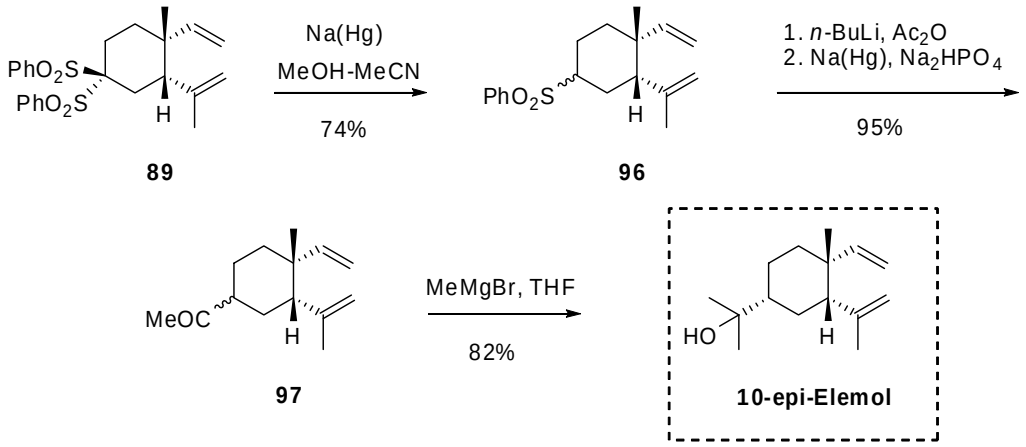
Z = SO_2Ph

Scheme 57

106 The potential of metal-promoted allyl/allyl couplings for the construction of sesquiterpenes had previously been demonstrated by Corey by using a $Ni(CO)_4$ promoted cyclization which proceded with low regio- and stereoselectivities: Corey, E. J.; Broger, E. *Tetrahedron Lett*. **1969**, *20*, 1779-1782.

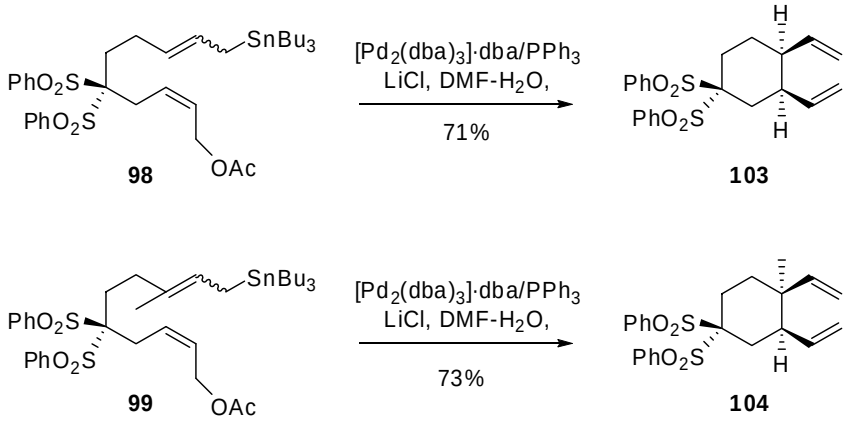
The reaction proceeded in a highly stereoselective manner to provide exclusively *cis*-dialkenyl cyclohexane **89** in good yield.[107] The presence of a bis(η^3-allyl)palladium complex intermediate in the catalytic cycle was strongly supported by the formation of the same carbocycle **89** from allylstannane **95** (Scheme 57).[108]

The configuration of carbocycle **89** was unambiguously determined by its transformation into naturally occurring 10-epi-elemol (Scheme 58).



Scheme 58

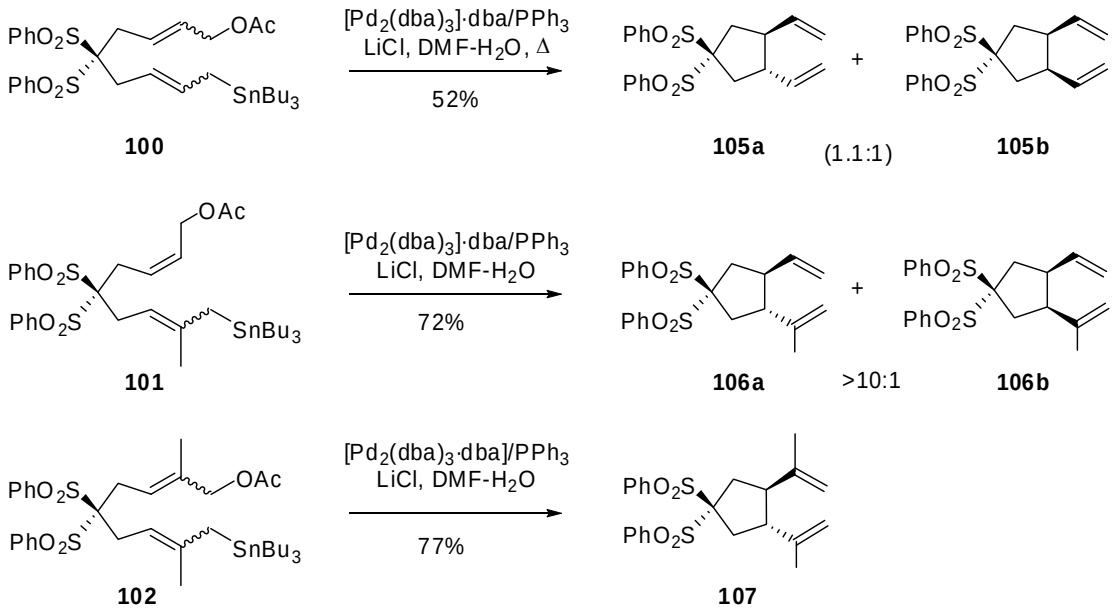
Cyclization of allylstannanes by treatment with allyl acetates is a general reaction as shown in Schemes 59a and 59b. Thus, substrates **98-102** cyclize at 80 ºC to afford carbocycles **103-107.**



Scheme 59a

107 Cuerva, J. M.; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. *J. Org. Chem.* **1997**, *62,* 7540-7541.

108 Cuerva, J. M. *Doctoral Thesis*, UAM, **1997**.



Scheme 59b

This intramolecular Stille coupling is stereoselective, regardless of the configuration of the double bonds in the starting compounds. It appears that a strong bias exists towards the formation of *cis* six-membered rings and *trans* five-membered rings. Thus, treatment of **98** and **99** stereoselectively provided **103** and **104**, respectively, with the two *cis*-vinyl groups. Cyclization of **100**, however, gave a 1.1:1 mixture of *trans* and *cis* isomers **105a** and **105b**. A better selectivity was obtained in the cyclizations of **101** and **102**, which gave *trans* derivatives as the major compounds (Scheme 59).[109]

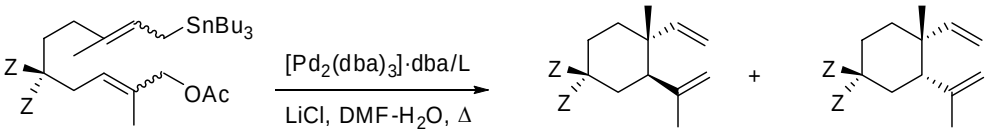
The cyclization of **94** was studied in more detail.[110] This reaction could also be performed in the absence of PPh_3, although the reaction required a stoichiometric amount of palladium. Monodentate phosphines (PCy_3, $P(2\text{-fur})_3$, (di-phenylphosphanyl)ruthenocene), phosphites ($P(OMe)_3$, $P(O\textit{i}Pr)_3$, $P(OPh)_3$, $P(OCH_2)_3CEt$),[111] and $AsPh_3$ gave exclusively *cis*-**89**. The cyclization did not take place with other common bidentate ligands (dppm, dppp, and dppb), while dppe led to **89** in

109 Méndez, M.; Echavarren, A. M. *Eur. J. Org. Chem*. **2002**, 15-28.

110 Méndez, M. *Doctoral Thesis*, UAM, **2001**.

111 (a) Serron, S. A.; Luo, L.; Stevens, E. D.; Nolan, S. P.; Jones, N. L.; Fagan, P. J. *Organometallics* **1996**, *15*, 5209-5215. (b) Stahl, L.; Trakarnpruk, W.; Freeman, J. W.; Arif, A. M.; Ernst, R. D. *Inorg. Chem.* **1995**, *34*, 1810-1814. (c) Ernst, R. D.; Freeman, J. W.; Stahl, L.; Wilson, D. R.; Arif, A. M.; Nuber, B.; Ziegler, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 5075-5081.

only 47% yield. Interestingly, the reaction could be performed with dppf or the related dppr (1,1'-bis(diphenylphosphino)ruthenocene)[112] as the ligands to give a 1:3 (100%) or 1:5.3 (93%) mixture of the *trans* and *cis* isomers of **89** (Scheme 60).

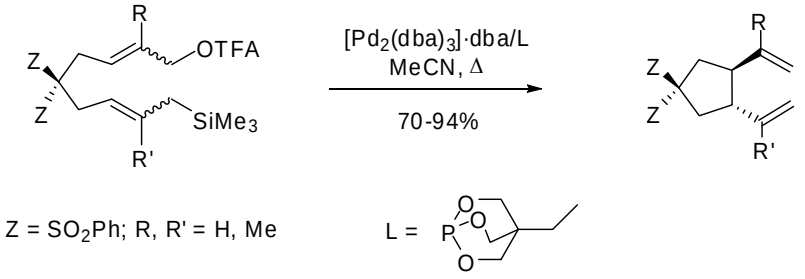


Z = SO_2Ph

L	Yield(%)	ratio **89a/89b**
dppf	100	1:3
dppr	93	1:5.3

Scheme 60

This reaction could be extended to allylsilanes, but in this case only trifluoroacetates are reactive and a bicyclic phosphite was the only suitable ligand (Scheme 61).



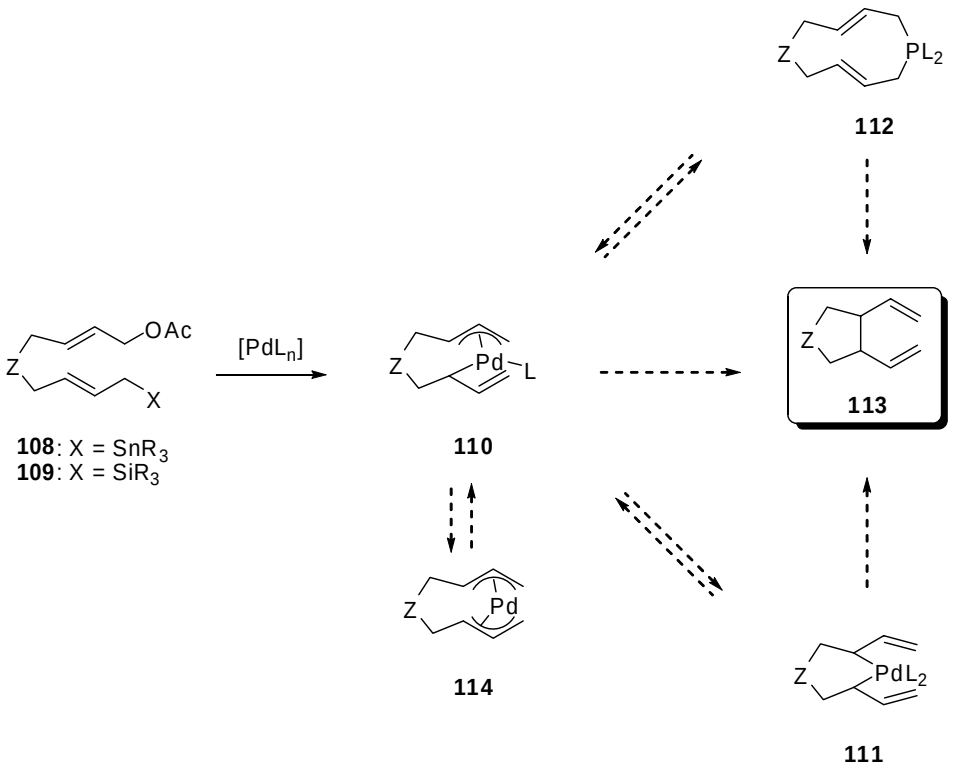
Z = SO_2Ph; R, R' = H, Me

Scheme 61

Although less general than the reaction of allyl stannanes, the carbocyclizations of allyl silanes proceed with high stereoselectivity. In contrast to the Oppolzer cyclization, in the cyclizations of allylstannanes and allylsilanes, methyl substitution at the C-2 or C-3 positions on either the nucleophilic or the electrophilic allyl moieties is possible, and the corresponding carbocycles are obtained in better yields than with the unsubstituted substrates.

The mechanism leading to the formation of the C-C bonds in these cyclizations was studied by density functional theory (DFT) calculations.[95] In Scheme 62 all the possible reductive pathways for the formation of carbocycles **113** are depicted.

112 Li, S.; Wei, B.; Low, P. M. N.; Lee, H. K.; Hor, T. S. A.; Xue, F.; Mak, T. C. W. *J. Chem. Soc., Dalton Trans.* **1997**, 1289-1293.



Scheme 62

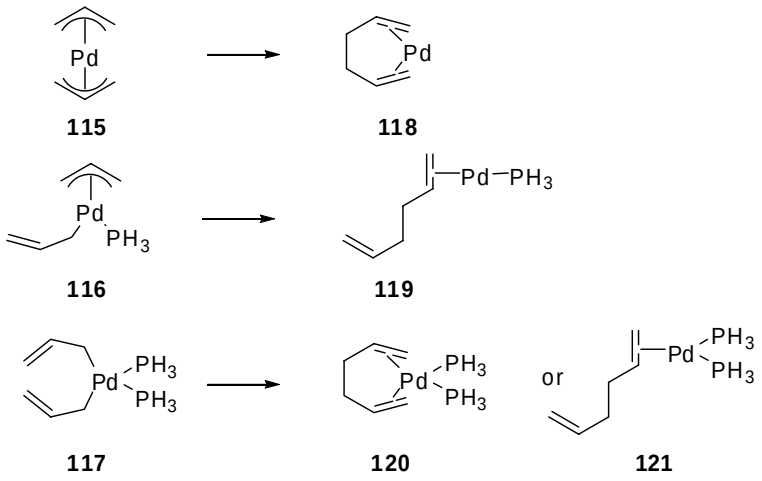
Intramolecular transmetalation[113] of the (η^3-allyl)palladium complexes formed by oxidative addition of allyl acetates to Pd(0) would initially form complexes of type **110**. Subsequent rapid equilibration might form bis(η^1-allyl)palladium complexes **111** and/or **112**, as well as bis(η^3-allyl)palladium complexes **114**.

The reductive elimination process might take place starting from bis(η^3-allyl)-, (η^1-allyl)(η^3-allyl)-, or bis(η^1-allyl)palladium complexes. Hence, complexes **115-117** (Scheme 63) were used as models for the reagents involved in the reductive elimination in the DFT studies leading to (1,5-hexadiene)palladium complexes **118-119**, respectively.

The possible mechanisms for the reductive elimination were compared by determining the corresponding activation energies. From the results, it could be concluded that the preferred pathway for the intramolecular allyl/allyl coupling is the formation of the C-C bond between the C-3 terminus of the allyl ligands of a bis(η^1-

113 Mechanisms of Stille coupling reactions: (a) Casado, A. L.; Espinet, P. *J. Am. Chem. Soc*. **1998**, *120*, 8979-8985. (b) Casado, A. L.; Espinet, P. Gallego, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 11771-11782. (c) Casado, A. L.; Espinet, P.; Gallego, A. M. Martínez-Ilarduya, *Chem. Commun.* **2001**, 339-340. (d) Albéniz, A. C.; Espinet, P.; Martín-Ruiz, B. *Chem. Eur. J*. **2001**, *7*, 2481-2489.

allyl)palladium complex **117**, which is in agreement with the fact that the cyclization of substrate **94** proceeds in the presence of bidentate ligands such as dppf and dppr.



Scheme 63

These results point to the formation of bis(η^1-allyl)palladium macrocycles of type **112** (Scheme 62) (or its *cis*,*trans* and *cis*,*cis* stereoisomers) as the most reactive species for the last step in the cyclization reactions when phosphane complexes are present in the reaction medium. It is important to note that these conclusions pertain to the coupling in the presence of donor phosphine ligands. In the absence of such ligands,[114] other mechanisms might operate.

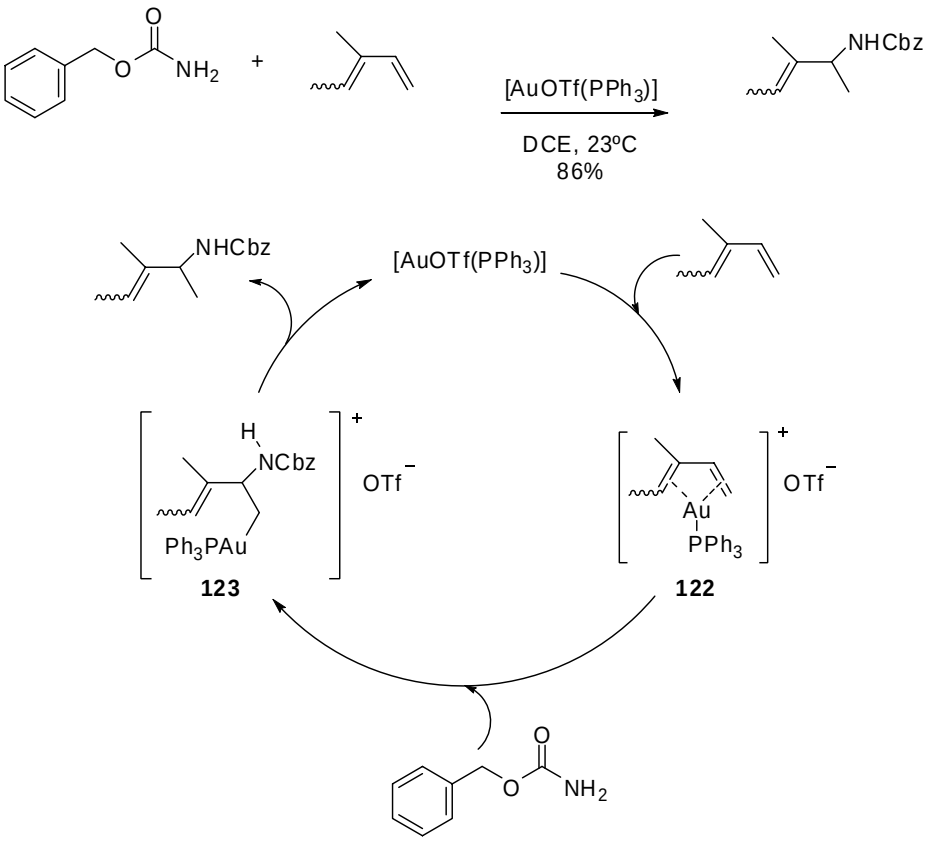
3. Gold activation of alkenes

Gold-catalyzed reactions have emerged as important synthetic methods.[115] Au(I) and Au(III) are soft π-acids, and are in principle capable of activating all C-C-π systems (alkenes, dienes, alkynes, allenes and arenes). Whilst nucleophilic addition to a metal-activate alkyne offers a diverse range of reaction outcomes, the analogous transformation with alkenes leads generally to 1,2-addition.

114 (a) Goliaszewski, A.; Schwartz, J. *Organometallics* **1985**, *4*, 417-419. (b) Goliaszewski, A.; Schwartz, J. *Tetrahedron* **1985**, *41*, 5779-5789. (c) Bertani, R.; Berton, A.; Carturan, G.; Campostrini, R. *J. Organomet. Chem*. **1988**, *349*, 263-268.

115 For recent rewiews, see: (a) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun*. **2007**, 333-346. (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal*. **2006**, *348*, 2271-2296. (c) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem. Int. Ed*. **2006**, *45*, 7896-7936. (d) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed*. **2007**, *46*, 3410-3449.

Hydroamination of 1,3-dienes is efficiently catalyzed by gold(I) to yield allylic amines,[116] which are important precursors in organic synthesis (Scheme 64). The reaction takes place under very mild conditions using carbamates and sulfonamides as nucleophiles.[117]



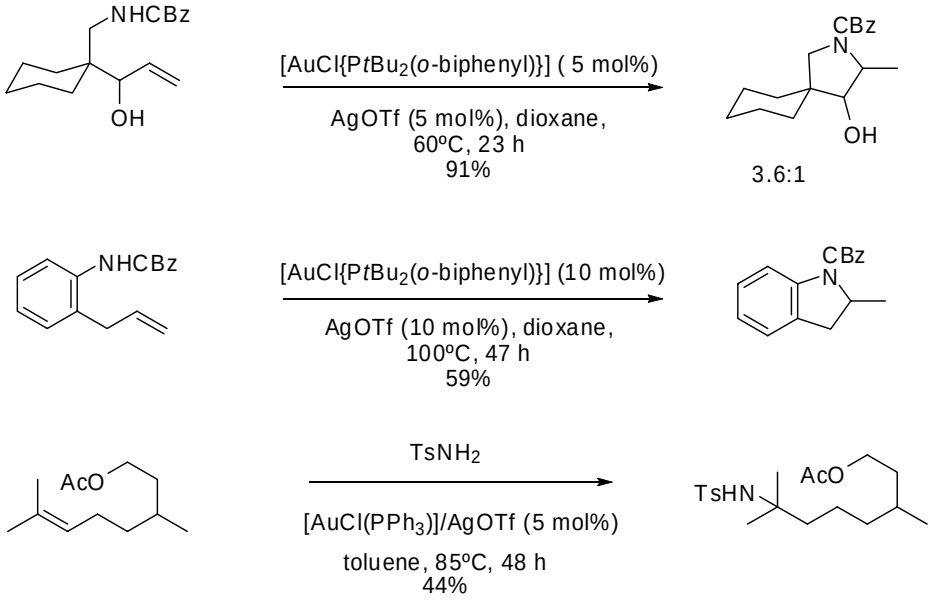
Scheme 64

The proposed reaction mechanism involves the coordination of a cationic gold(I) complex to the diene to form **122**. This is based on the shift of the ^{31}P signal observed after the addition of the diene. Thereafter, the nucleophile attacks *anti* to the gold center. The resulting Au(I)-C bond in **123** is then protonated to give the desired product and to regenerated the active catalyst.

116 For a review on allylic amination see: Johannsen, M.; Jorgensen, K. A. *Chem. Rev*. **1998**, *98*, 1689-1708.

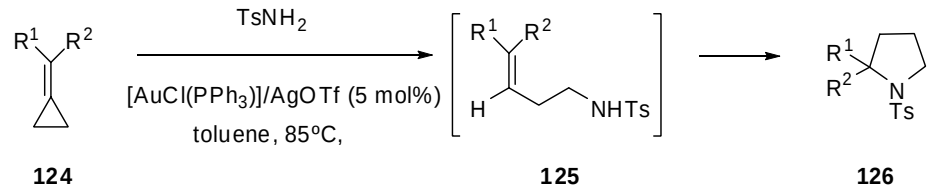
117 Brouwer, C.; He, C. *Angew. Chem. Int. Ed*. **2006**, *45*, 1744-1747.

Hydroamination of unactivated olefins can be catalyzed as well by gold complexes to afford acyclic or cyclic nitrogen-containing molecules (Scheme 65).[118] Thus, tosyl-amides react with different olefins to afford Markovnikov addition products without suffering β-hydride elimination. Other nitrogen-based molecules, such as amines, anilines, carboxyamides, carbamates, alkylsulfonamides, or sulfamates failed to react or give low yield. The intramolecular version of the reaction takes place also with carbamates as nucleophiles. This protocol can be applied to the synthesis of aromatic and aliphatic heterocyclic compounds and to the synthesis of piperidine derivatives.



Scheme 65

A recent example combined gold-catalyzed hydroamination with the *in situ* generation of the required homoallylic amine precursor by a ring-opening coupling of an amine and a methylenecyclopropane (Scheme 66). [119]



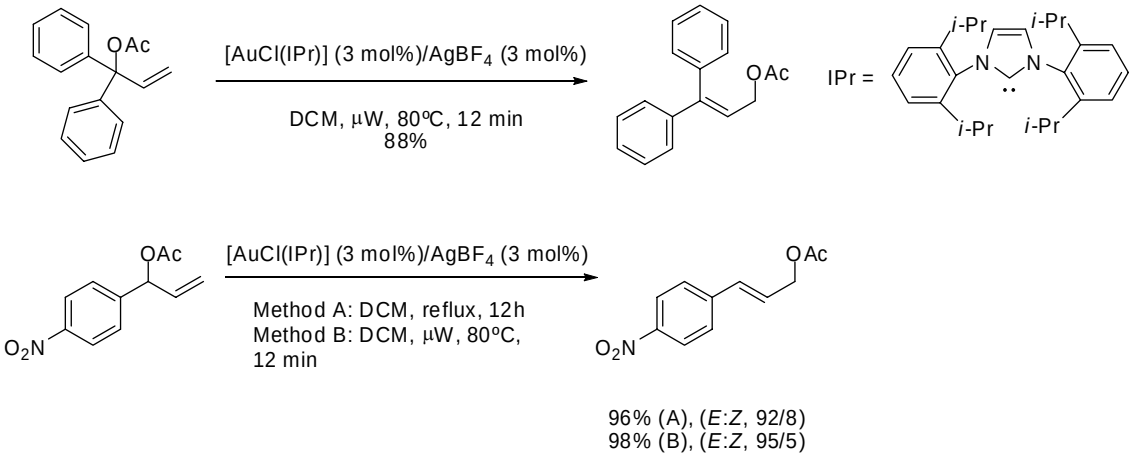
Scheme 66

118 (a) Zhang, J.; Cai-Guang, Y.; He, C. *J. Am. Chem. Soc*. **2006**, *128*, 1798-1799. (b) Han, X.; Widenhoefer, R. A. *Angew. Chem. Int. Ed*. **2006**, *45*, 1747-1749. (c) Rosenfeld, D. C.; Shekhar, S.; Takemiya, A.; Utsunomiya, M.; Hartwitg, J. F. *Org. Lett*, **2006**, *8*, 4179-4182.

119 Shi, M.; Liu, L.-P.; Tang, J. *Org. Lett*. **2006,** *8*, 4043-4046.

Only traces of the ring-opening product **125** were detected, whereas various Lewis acids promoted the ring-opening reaction of **124** to give **125** as major product. For methylenecyclopropanes **124** substituted by a single aromatic group, the reactions proceed smoothly to give the corresponding pyrrolidine derivatives **126** in 34-76%.

Very recently, an allylic isomerization of secondary and tertiary allyl acetates has been described. This was catalyzed by gold(I) complexes with N-heterocyclic carbene ligands.[120] The reaction proceeds under thermal or microwave-assisted conditions to yield primary allyl acetates (Scheme 67).



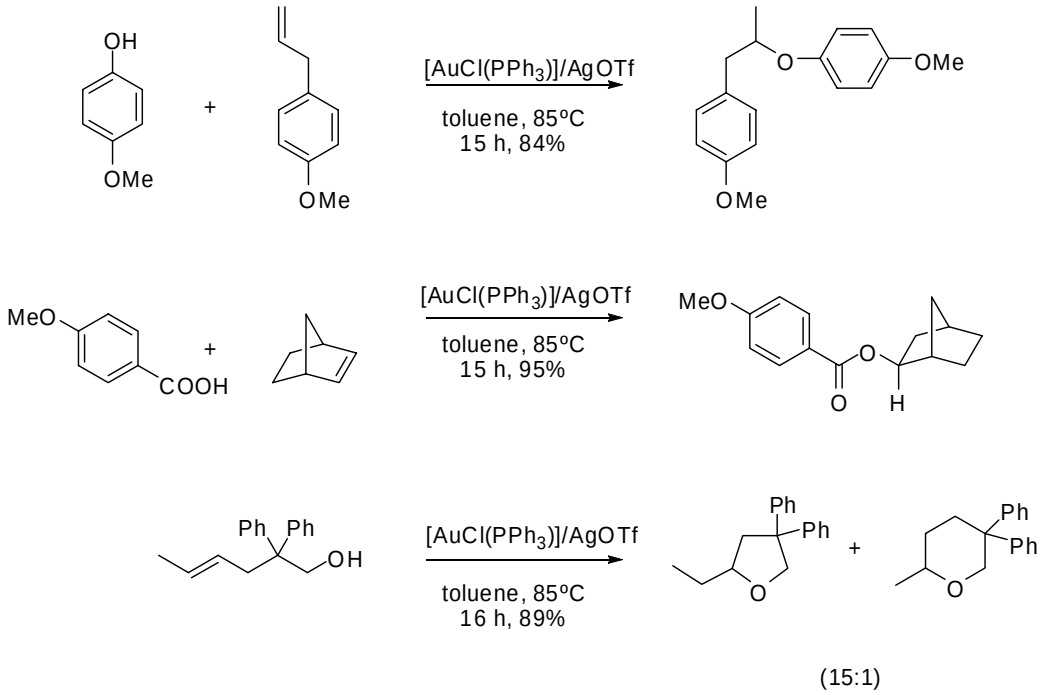
Scheme 67

For the isomerization process the authors proposed a π-coordination of the alkene moiety to the cationic gold center which triggers an intramolecular nucleophilic attack of the carbonyl leading to a stabilized 1,3-acetoxonium. Completion of the 1,3-shift of the acetate would produce the isomerized olefin. An analogue isomerization of allenyl esters to 1,2-butadien-2-ol esters catalyzed by gold(I) has been proposed to proceed through the same acetoxonium intermediate.[121]

120 Marion, N.; Gealageas, R.; Nolan, S. P. *Org. Lett*. **2007**, *9*, 2653-2656.

121 Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Org. Lett*. **2007**, *9*, 985-988.

There are only a few examples of addition of oxygen nucleophiles like phenols and carboxylic acids to simple olefins catalyzed by gold.[122] In these cases, gold acts as a simple Lewis acid only coordinating to the olefin and generating an incipient carbon cation that traps weak nucleophiles.



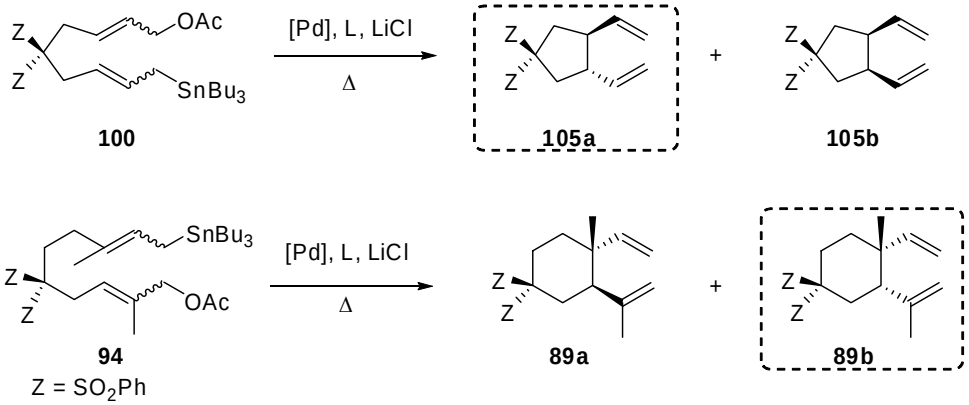
Scheme 68

122 (a) Cai-Guang, Y.; He, C. *J. Am. Chem. Soc*. **2005**, *127*, 6966-6967. (b) Li, Z.; Zhang, J.; Chad, B.; Cai-Guang, Y.; Reich, N. W.; He, C. *Org. Lett*. **2006**, *8*, 4175-4178.

Chapter 1. Objectives

Objectives

As was described in the Introduction in section 2.3, five-(**105a/105b**) and six-membered ring carbocycles (**89a/89b**) can be obtained by the intramolecular allyl/allyl coupling of substrates of type **100** and **94**.[95,109] The reaction is stereoselective regardless of the configuration of the double bonds in the starting compounds. Interesting is that five-membered rings are mainly obtain with a *trans* configuration while six-membered rings are mainly obtained with a *cis* configuration (Scheme 69).



Scheme 69

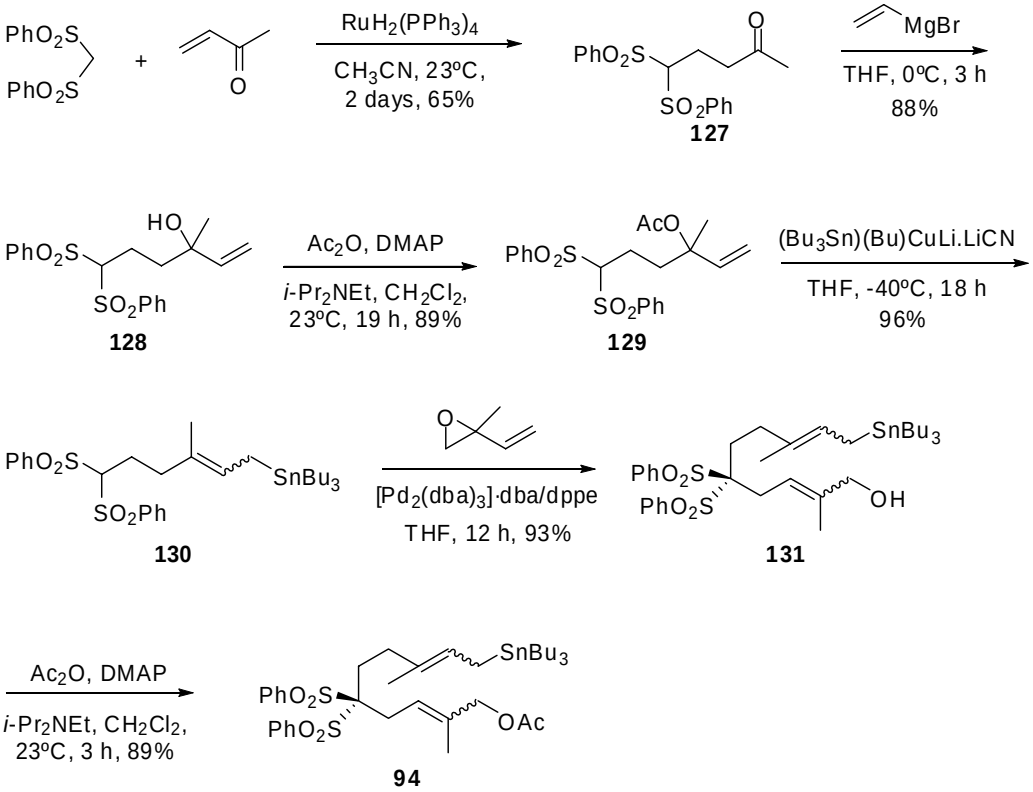
Although the general mechanistic aspects of the cyclization reaction were well understood from the previous work carried out in the group, the stereochemistry of the process was difficult to justify. Moreover, the synthesis of *trans*-six-membered ring carbocycles is of interest because they posses the same configuration at the cyclohexane ring as lobane diterpenes, marine natural products with potent anti-inflammatory activity.

The first objective of this Doctoral Thesis was therefore to find conditions that would allow reversing the preferred stereoselectivity observed in the palladium-catalyzed cyclization of substrates of type **94**. It was also of interest to search for other metals as catalysts in these cyclizations that would lead to more selective couplings or with different stereo- and/or regioselectivities.

Chapter 1. Results and Discussion

1. Studies directed towards the synthesis of six-membered ring carbocycles with *trans*-1,2-dialkenyl configuration

Compound **94** was chosen as the required precursor for the cyclization reaction. Its synthesis was accomplished in six steps following the synthetic pathway previously described for the synthesis of epi-elemol (Scheme 70).[107] The first step is a Michael addition developed in our group[123] catalyzed by a ruthenium dihydride. Reaction of keto disulfone **127** with vinylmagnesium bromide affords alcohol **128** which after acetylation gives acetate **129**. This compound was transformed into the corresponding allylstannane using the methodology developed by Lipshutz.[124] The second alkyl chain was introduced by nucleophilic attack of stannane **130** to isoprene epoxide catalyzed by palladium. Finally, acetylation of **131** affords **94** that was obtained as a mixture of *E*/*Z* isomers in both allyl moieties.



Scheme 70

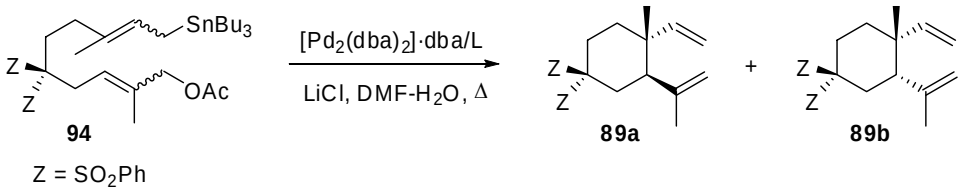
107 Cuerva, J. M.; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. *J. Org. Chem.* **1997**, *62,* 7540-7541.

123 Gómez-Bengoa, E.; Cuerva, J. M.; Mateo, C.; Echavarren, A. M. *J. Am. Chem. Soc*. **1996**, *118*, 8553-8565.

124 Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett*. **1989**, *30*, 2065-2068.

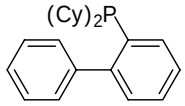
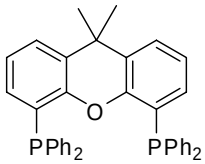
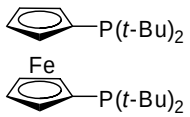
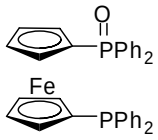
From a theoretical study concerning the allyl/allyl coupling,[95] it was found that the reductive elimination takes place from a bis(η^1-allyl)palladium complex with two donor ligands L or one bidentated ligand L_2. If phosphine ligands are involved in the cyclization step, they might affect the stereochemical course of the reaction. In fact, preliminary results showed that the *trans* isomer was observed, although as a minor compound, when the reaction takes place with the bidentate ligands 1,1'-bis(diphenylphosphine)ferrocene (dppf) and 1,1'-bis(diphenylphosphine)ruthenocene (dppr).[110] For this reason, we decided to study the effect of other phosphines in this reaction (Table 1).

Table 1. Influence of the ligand on the stereoselectivity.



94 **89a** **89b**

Z = SO_2Ph

Entry	L	Yield(%)	89a/89b
1		30	0:1
2		30	0:1
3		69	0:1
4		78	0:1

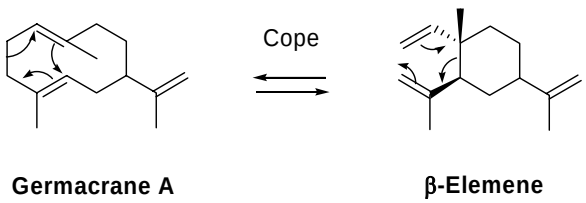
Steric hindrance and a large bite angle in the phosphine compounds lowered the yield of the reaction and led exclusively to the formation of the *cis* isomer (entries 1-3).

95 Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 3620-3628.

110 Méndez, M. *Doctoral Thesis*, UAM, **2001**.

The monoxide dppf was tested as well, as this might be generated *in situ* by oxidation of dppf. Bis-phosphine monoxides are hemilabile ligands with soft (P) and hard (O) nucleophilic centers within the same ligand, thus conferring special properties to metals.[125] However, the use of dppf monoxide had no consequence on the stereoselectivity of the reaction although **89b** was obtained in good yield (Table1, entry 4).

A different approach to reverse the stereoselectivity of the product was based on the different thermodynamic stability of the *cis* and *trans* isomers. Germacrenes are a family of monocyclic terpenes structurally related to the elemanes, and that are believed to be their biosynthetic precursors. In fact, germacrane A it is known to undergo a thermal Cope rearrangemen to β-elemene[126] (Scheme 71). On the basis that the *trans* isomer should be thermodynamically more stable than the *cis*, it should be possible to isomerize the *cis* isomer to the *trans* via equilibration through a ten membered intermediate generated by a Cope rearrangement.



Scheme 71

The Cope rearrangement of 1,5-dienes is promoted by $PdCl_2$.[127] The typical conditions use $[PdCl_2(MeCN)_2]$ as catalyst in THF at room temperature. When a 3:1 mixture of *trans/cis* isomers (**89a** and **89b**) was submitted to these reaction conditions, the ratio remained unchanged even after being heated to reflux for 24 h (Table 2, entry 1). A more electrophilic palladium complex also failed to increase the amount of *trans*

125 Grushin, V. V. *J. Am. Chem. Soc*. **1999**, *121*, 5831-5832 and references therein.

126 De Kraaker, J. W.; Franssen, M. C. R.; de Groot, A.; Koening, W. A.; Bouwmeester, H. J. *Plant. Physiol*. **1998**, *117*, 1381-1392.

127 (a) Trebellas, J. C.; Olechowski, J. R.; Jonassen, H. B. *J. Organomet. Chem*. **1966**, *6*, 412-420. (b) Heimbach, P.; Molin, M. *J. Organomet. Chem*. **1973**, *49*, 477-482. (c) Overman, L. E.; Knoll, F. M. *J. Am. Chem. Soc*. **1980**, *102*, 865-867. (d) Overman, L. E.; Jacobsen, E. J. *J. Am. Chem. Soc*. **1982**, *104*, 7225-7231. (e) Bluthe, N.; Malacria, M.; Gore, J. *Tetrahedron. Lett*. **1983**, 1157-1160. (f) Overman, L. E.; Renaldo. A. F. *Tetrahedron. Lett*. **1983**, 2235-2238. (g) Overman, L. E.; Renaldo, A. F. *Tetrahedron. Lett*. **1983**, 3757-3760.

isomer (Table 2, entry 2). Finally, the isomeric mixture was treated for three days under the standard carbocyclization conditions leading only to the unchanged 3:1 ratio of the *cis*/*trans* mixture (Table 2, entry 3).

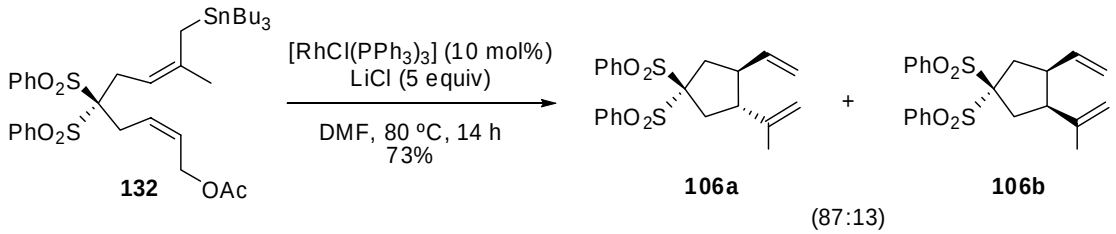
Table 2. Results after subjecting **94** to isomerization conditions.

Entry	Initial ratio *cis*/*trans*	Catalyst	Solvent	t(h)	Final ratio *cis*/*trans*
1	3:1	$[PdCl_2(MeCN)_2]$	THF[a]	24	3:1
2	3:1	$[Pd(MeCN)_4](BF_4)_2$	THF[a]	24	3:1
3	3:1	$[Pd_2(dba)_3]$·dba, dppf ,LiCl	DMF[b]	72	3:1

(a) reflux. (b) 90ºC.

2. Rhodium-catalyzed cyclizations of allylstannanes with allylacetates

Parallel to the search for the conditions which lead to *trans*-1,2-dialkenyl six-membered rings by palladium catalysis, we undertook a study on the application of other metals for the cyclizations of allylstannanes with allylacetates. We found that the electron-rich Rh(I) complex $[RhCl(PPh_3)_3]$ was able to perform the cyclization under similar conditions to those that were employed for the catalysis with Pd(0) (Scheme 72).



Scheme 72

The stereochemistry of the process was similar to that observed with Pd(0), but the results were very interesting since this intramolecular cross-coupling reaction catalyzed by Rh(I) had no precedent. Recently, much attention has been given to Rh(I)-catalyzed processes.[128] Although organoboranes are mostly used as nucleophiles, in a

128 Reviews on Rh-ctalyzed couplings: (a) Fagnou, K.; Lautens, M. *Chem. Rev*. **2003**, *103*, 169-196. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev*. **2003**, *103*, 2829-2844. (c) Miura, T.; Murakami, M. *Chem. Commun*. **2007**, 217-224.

few applications organostannanes have also been employed.[129] However, no example of reaction allylstannanes have been reported. For these reasons, we decided to study the scope and limitations of this process in more detail.

To determine whether or not the observed reactivity depend on the configuration of the double bounds, well defined configuration regioisomers of **132** (**133-135**) were synthesized (Figure 5).

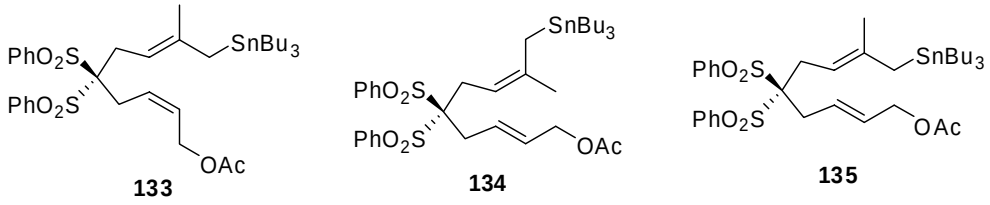
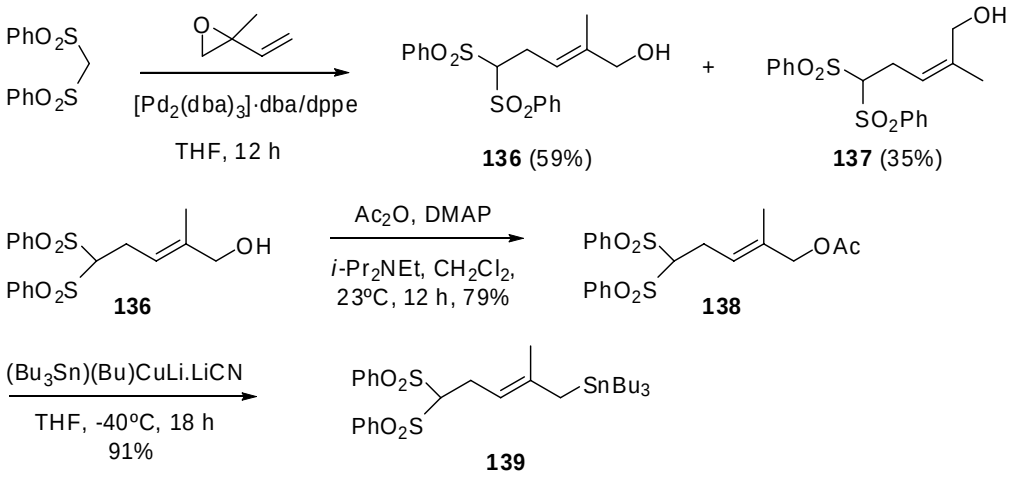


Figure 5

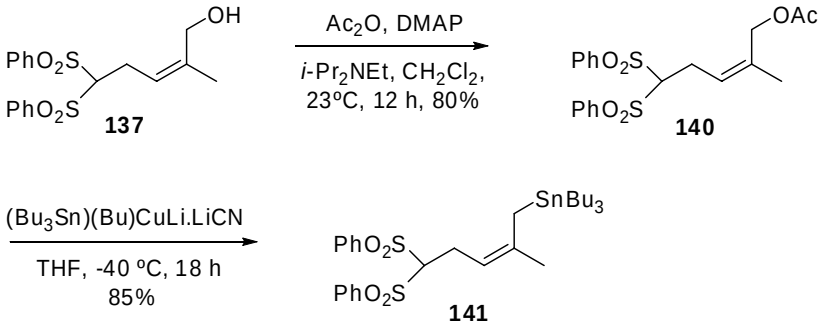
2.1. Synthesis of stereodefined precursors of five-membered ring carbocycles

Allylstannanes **132-135** had been prepared as a mixture of regioisomers in previous work.[95,109] Compounds with well defined configuration were obtained as shown in Schemes 73 and 74. Nucleophilic addition of bis(phenylsulfonyl)methane to isoprene epoxide gave rise to a mixture of *E*/*Z* allylic alcohols **136** and **137**, which were separated by chromatography. Acetylation of **136** and **137** afforded acetates **138** and **140**, which were transformed into the corresponding *E* and *Z* stannanes **139** and **141**, respectively.



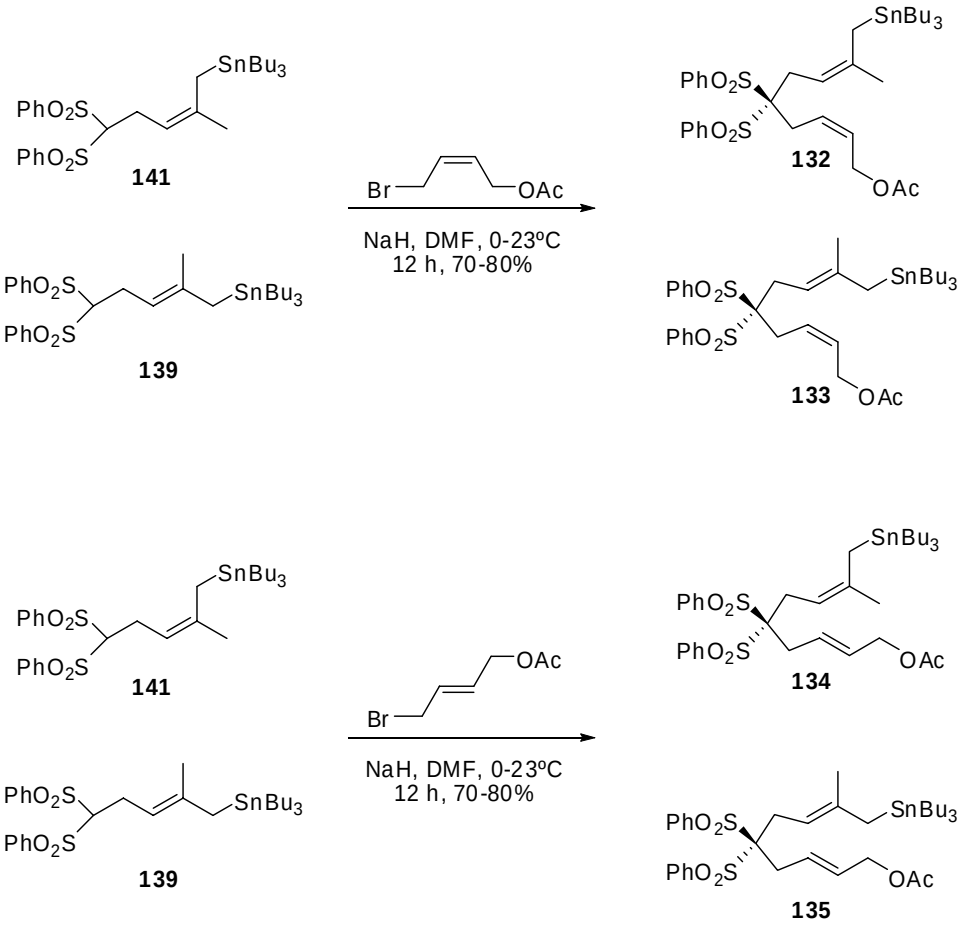
Scheme 73a.

129 (a) Oi, S.; Moro, M.; Inoue, Y. *Chem. Commun*. **1997**, 1621-1622. (b) Li, C.-H.; Meng, Y. *J. Am. Chem. Soc*. **2000**, *122*, 9538-9539. (c) Huang, T.; Meng. Y.; Venkatraman, S., Wang, D.; Li, C.-H. *J. Am. Chem. Soc.* **2001**, *123*, 7451-7452. (d) Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc*. **2000**, *122*, 976-977. (d) Hayashi, T.; Ishigedani, M. *Tetrahedron* **2001**, *57*, 2589-2595.



Scheme 73b.

The allyl acetate moiety was introduced by alkylation with (*E*)-1-acetoxy-4-bromo-2-butene[130] or (*Z*)-1-acetoxy-4-bromo-2-butene,[131] prepared independently. By this procedure, substrates **133-135** were obtained as single diasteromers (Scheme 74).



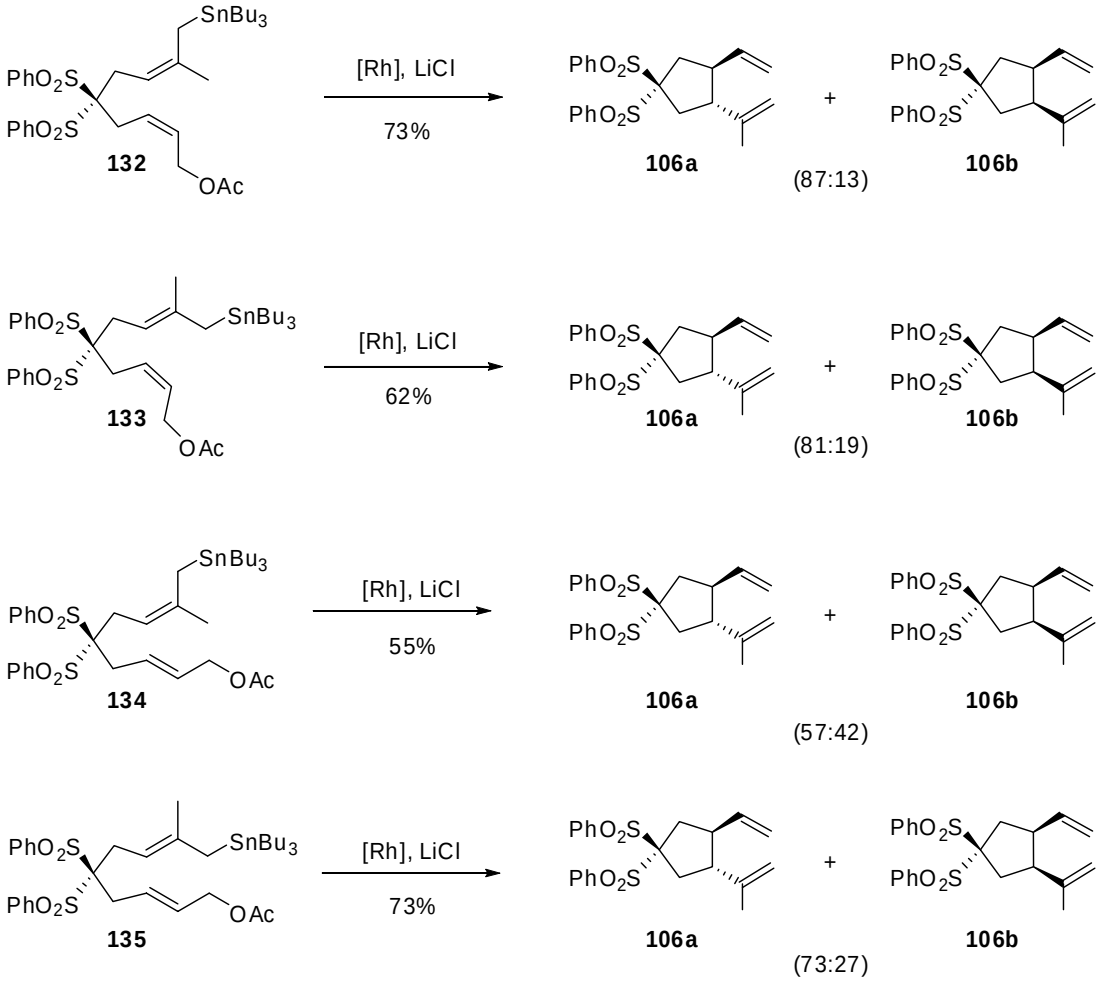
Scheme 74

130 Organ, M. G.; Cooper, L. R.; Soleymanzadeh, F.; Paul, T. *J. Org. Chem*. **2000**, *65*, 7959-7970.

131 Reppe, W. *J. Liebigs Ann. Chem*. **1955**, 80-158.

2.2. Cyclization reactions with [RhCl(PPh$_3$)$_3$]

The reaction of substrates **133-135** with [RhCl(PPh$_3$)$_3$] was performed under the same conditions used for the cyclization of **132** (Scheme 75). The carbocycle bearing *trans*-1,2-dialkenyl substituents was the major stereoisomer obtained in all cases, as occurred with this type of compounds in the catalysis with Pd(0). Nevertheless, the stereoselectivity and yield depended on the configuration at the double bonds. It was observed that substrates with an *E* configuration at the allyl acetate were less reactive. In these cases, the conversion was not complete even after heating at 80ºC for 14 h (88% for **134** and 84% for **135**). Lower yield and diastereoselecitvity was obtained for substrate **134**.

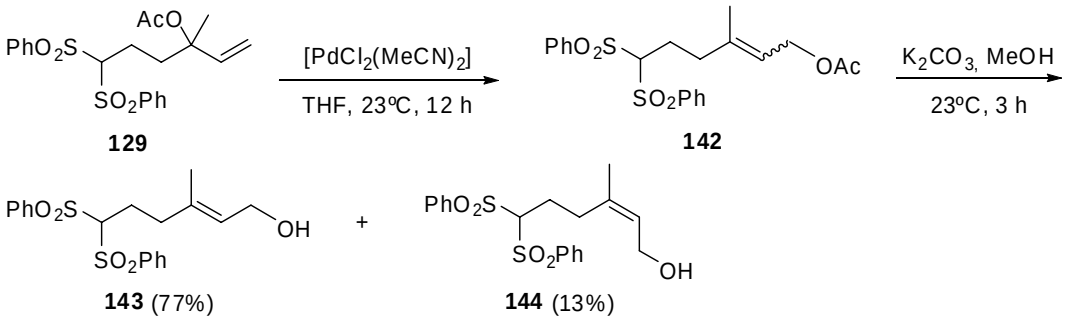


Scheme 75. [Rh] = [RhCl(PPh$_3$)$_3$] (10 mol%), LiCl (5 equiv), DMF, 80ºC, 14 h.

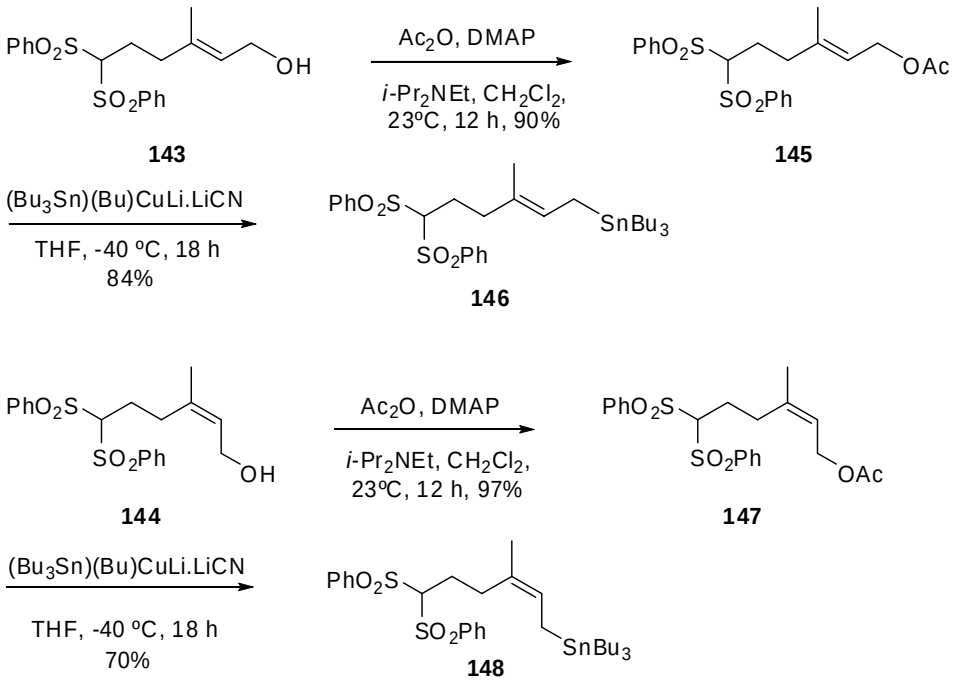
From the results above it was of interest to study the cyclization of substrates which can form six-membered ring carbocycles with sterodefined samples. In particular, we focus on the cyclization of **94**, as this is the precursor for the synthesis of the lobane diterpenes.

2.3. Synthesis of stereodefined precursors of six-membered ring carbocycles

In order to obtain substrates with *E* and *Z* configurations at the allyl moieties, analogs of **94** were prepared by a modified procedure depicted in Schemes 76, 77 and 78. Allylacetate **129** was submitted to an allylic isomerisation catalyzed by Pd(II).[132] The mixture of *E*/*Z* allylic acetates (**142**) obtained was then transformed into the corresponding alcohols **143** and **143**, which were separated by chromatography. The stannanes were introduced via the standard procedure (Scheme 77)



Scheme 76

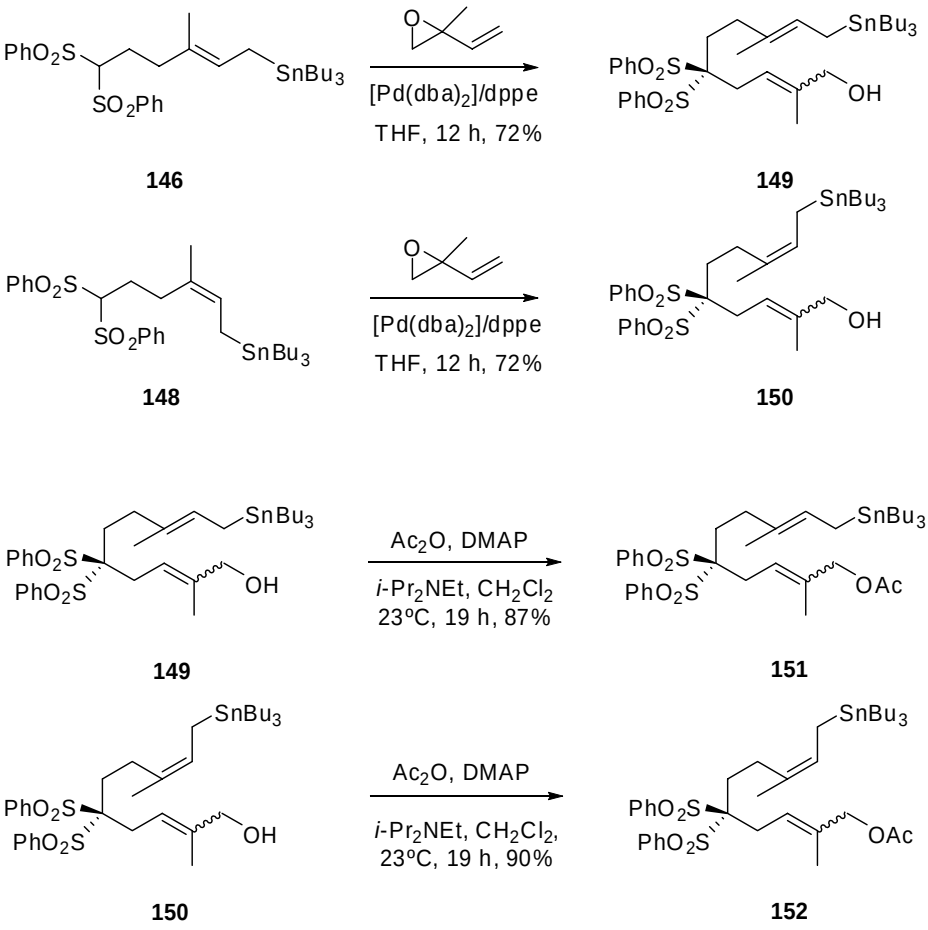


Scheme 77

The allyl acetate units were introduced by reaction of **146** and **148** with isoprene epoxide and subsequent acetylation of the hydroxyl groups. Unfortunately, the *E* and *Z* isomers of the allyl acetates could not be separated by chromatography (Scheme 78). As

132 Overman, L. E.; Knoll, F. M. *Tetahedron Lett*. **1979**, *4*, 321-324.

a result, allylstannanes **151** and **152** were obtained as a mixture of *E*/*Z* isomers at the allyl acetate chains.



Scheme 78

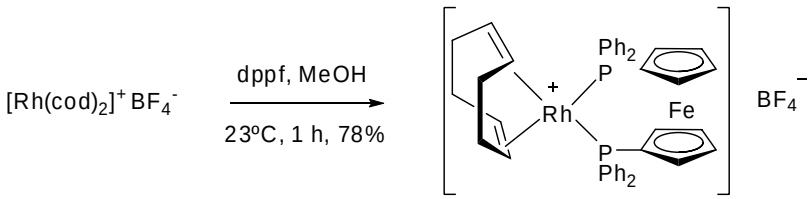
2.4. Rh(I)-catalyzed cyclization reactions of 94, 151 and 152

Substrates **94**, **151** and **152** were treated with $[RhCl(PPh_3)_3]$ as catalyst under the same conditions used for cyclization of five-membered ring carbocycles. However all substrates failed to undergo cyclization. Changing the solvent to THF, dioxane and NMP did not improve the results. Neither did the use of CsF or CuI instead of LiCl as additive. Modification of $[RhCl(PPh_3)_3]$ with π-acceptor ligands such as $P(OMe)_3$ (Evans conditions for allylic alkylation)[31a] led to decomposition of the starting substrates.

In order to find a more general method for the Rh-catalyzed cyclization of allylstannanes with allyl acetates, various Rh(I) complexes were studied for the cyclization reaction.

31a Nelson, J. D.; Evans, P. A. *Tetrahedron Lett*. **1998**, *39*, 1725-1728.

The complex $[RhCl(cod)]_2$[133] is a general precursor for various Rh(I) catalysts as it allows easy introduction of different ligands. From it, two Rh(I) cationic complexes were prepared: $[Rh(cod)_2]BF_4$[134] and $[Rh(cod)dppf]BF_4$ (**153**). Complex **153**, was prepared by adding dppf to $[Rh(cod)_2]BF_4$ following a reported procedure for the synthesis of related cationic rhodium complexes with bidentate phosphines.[135] Its structure was confirmed by X-ray crystal structure determination (Figure 6). This complex, have a square-planar Rh center structure. The angle P-Rh-P was found to be 96.52º, whereas the angle C36-Rh-C41 angle was 76.96º. The distances Rh-P4, Rh-P3 were 2.36, 2.32Å and the distances Rh-C36, Rh-C41 were 2.27, 2.21Å, respectively.



153

Scheme 79

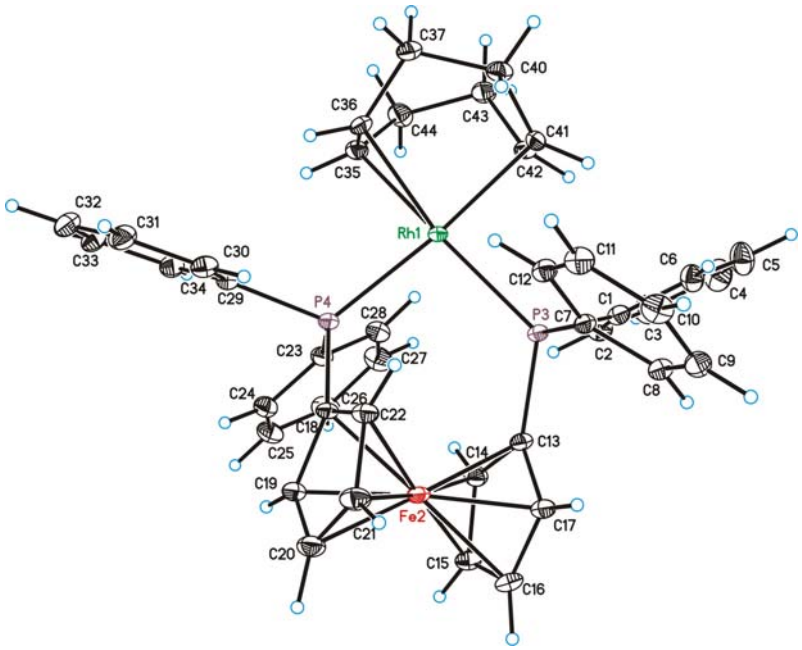


Figure 6. X-ray crystal structure of the cation of Rh(I) complex **153**.

133 Franz, R.; Kirchner, S.; Walter, R. EP 1116724, **2001**. *Chem. Abstr*. **2001**, *135*, 92754.

134 Schenck, T. G.; Downes, J. M.; Milne, C. R. C.; Mackenzie, P. B.; Boucher, H.; Whelan, J.; Bosnich, B. *Inorg. Chem*. **1985**, *24*, 2334-2337.

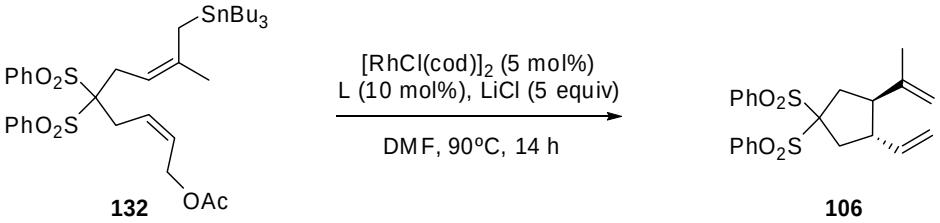
135 Hoge, Garrett; Wu, H.-P.; Kissel, W. S.; Pflum, D. A.; Greene, D. J.; Bao**,** J. *J. Am. Chem. Soc*. **2004**, *126***,** 5966-5967.

The activity of these complexes was tested with substrates **94**, **151** and **152** in DMF under various reaction conditions. Unfortunately, no cyclization was observed with these compounds. The starting material could be recovered in the case of complex **153** and $[RhCl(cod)]_2$ while $[Rh(cod)_2]BF_4$ led to decomposition.

2.5. Optimization of the Rh(I)-catalyzed cyclization

As the precursors for five-membered ring carbocycles generally gave better results, substrate **132** was chosen as a model to study the effect of adding different bidentate phosphines to $[RhCl(cod)]_2$. The reactions were performed under the same conditions that those employed with $[RhCl(PPh_3)_3]$. It was found that the yields were lower than in the case of $[RhCl(PPh_3)_3]$ (29-59%), and the diastereoselectivities were of the same order (see Table 3).

Table 3. Effect of bidentate phosphines.



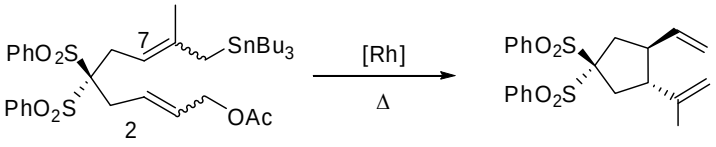
132 **106**

Entry	L	Conv%(Yield%)	*trans*/*cis*
1	dppp	100 (59)	86:14
2	dppe	90 (47)	81:19
3	dppm	56 (29)	83:17
4	dppf	52 (29)	75:25
5	Xantphos	66 (33)	72:28

Since decomposition of DMF to give CO in the presence of chloride salts has been used for the preparation of rhodium carbonyl complexes,[136] the activity of $[RhCl(CO)(PPh_3)_2]$ and $[RhCl(CO)_2]_2$ was also studied as related complexes may be generated *in situ* under the reaction conditions. The reactivity of these complexes as catalysts is compared with $[RhCl(PPh_3)_3]$ in Table 4.

136 Serp, P.; Hernandez, M.; Richard, B.; Kalck, P. *Eur. J. Inorg. Chem*. **2001**, 2327-2336.

Table 4. Results with Rh(I) carbonyl complexes.



133: 2*Z*, 7*E* **135:** 2*E*, 7*E*
134: 2*E*, 7*Z*

106a/b

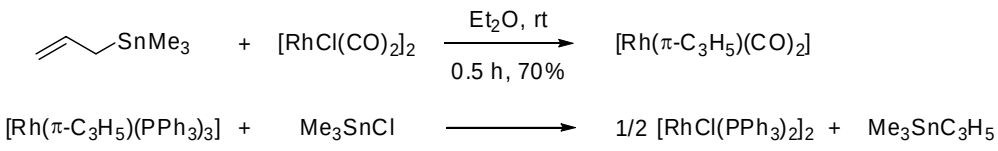
Entry	Substr.	Catalyst[a]	Additive(s)	Solvent	T(ºC)	t(h)	106 (%) (ratio a/b)
1	**134**	A	LiCl[b]	DMF	95	18	50 (66:34)
2	**134**	A	LiCl[b]	MeCN	70	18	20 (66:34)
3	**133**	A	LiCl[b]	THF	70	22	24 (70:30)
4	**135**	A	-	Toluene	80	18	-
5	**133**	B	LiCl[b]	THF	70	22	-
6	**134**	C	PPh_3[d]	DMF	95	18	21 (50:50)
7	**134**	C	PPh_3[d] LiCl[b]	THF	70	15	27 (76:24)
8	**133**	C	PPh_3[d] CsF[b]	THF	70	18	10[c]
9	**134**	C	PPh_3[d]	Toluene	80	69	23 (50:50)
10	**134**	C	PPh_3[d] $CsCO_3$[b]	THF	70	15	-
11	**134**	C	PCy_3[d]	Toluene	80	69	30 (76:24)
12	**134**	C	-	THF	70	18	Decomp.

(a) A = $[RhCl(CO)(PPh_3)_2]$, B = $[RhCl(PPh_3)_3]$, C = $[RhCl(CO)_2]_2$, 10 mol% of catalyst. (b) LiCl (3eq), CsF (3eq), $CsCO_3$ (3eq). (c) Determined by ^{1}HNMR. (d) (phosphine/catalyst) = 2:1. (e) 3 equiv.

The yields obtained in all cases were very low. The best result was obtained with $[RhCl(CO)(PPh_3)_2]$ as catalyst (Table 4, entry 1). With this catalyst the cyclization reaction also proceeded in THF and MeCN although in low yield (Table 4, entries 2 and 3), whereas $[Rh(PPh_3)_3Cl]$ was totally inactive in THF (entry 5). When the reactions were performed with $[Rh(CO)_2Cl]_2$ the yields were also low but it was found that LiCl was not essential for the reaction to proceed (entries 6, 9 and 11) whereas in the absence of LiCl no reaction at all was observed with $[RhCl(CO)(PPh_3)_2]$ (entry 4). The addition of LiCl, CsF or $CsCO_3$ to the reaction catalyzed by $[Rh(CO)_2Cl]_2$ did no improve the

yields (entries 7, 8 and 10), but the presence of a phosphine was necessary for the reaction to proceed, although the yield were also low (entries 6 and 12).

In these series of experiments with the carbocycles **106a/b,** were also isolated in low yield (8-9%) compounds arising from the destannylation of the starting material. The fact that these compounds were obtained was interesting because it suggests that the allylstannane first reacts with Rh(I) by transmetalation. Transmetalation of allylstannanes with Rh(I) has been reported before. In 1971 Abel et al. described the synthesis of π-allyldicarbonylrhodium(I) complexes using allyltrimethyltin as the source of π-allyl groups.[137] Interestingly, some years later Nixon et al. described the reverse reaction in which π-allylrhodim(I) complexes reacted with trimethyltin halides (Scheme 80).[138]



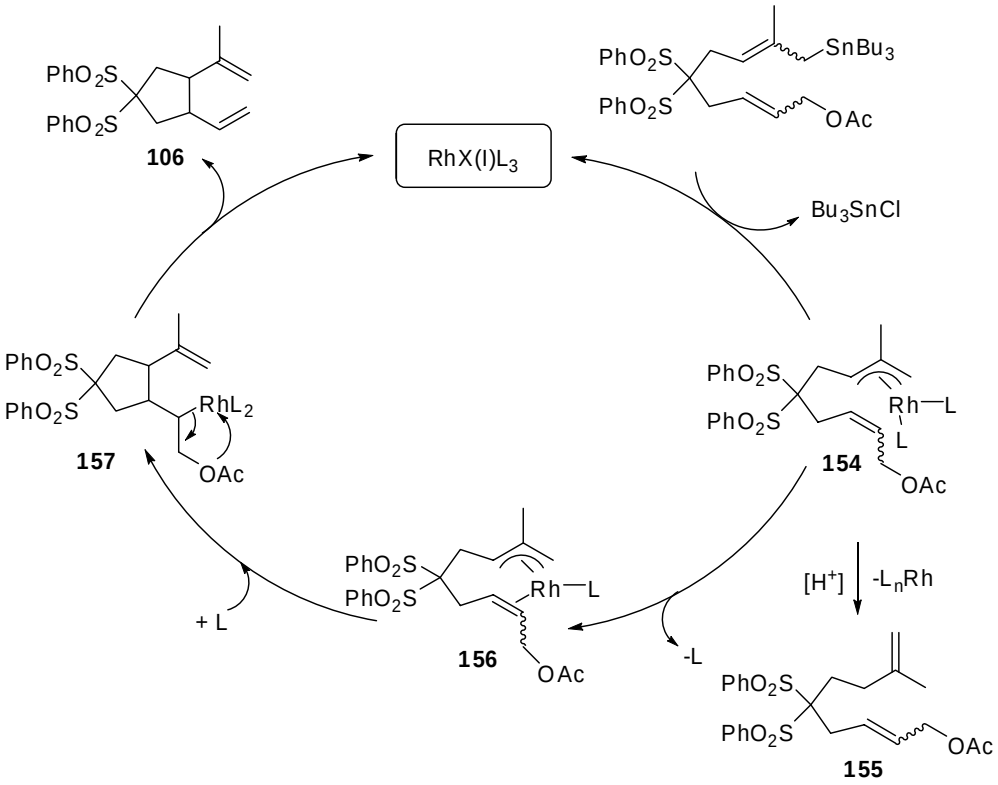
Scheme 80

According to these findings, a plausible reaction mechanism for the Rh(I) catalyzed cylization of allylstannanes with allylacetates is shown in Scheme 81. First a (η^3-allyl)Rh(I) complex **154** is generated by transmetalation of the initial Rh(I) complex with the allystannane moiety of the substrate. Complex **154** could suffer protodemetalation to form **155**. Coordination with the olefin generates **156** that undergoes migratory insertion to give **157**. At this stage, β-acetate elimination of Rh-OAc[139] from **157** would generate the carbocycle. In the proposed catalytic cycle no change in the oxidation state of Rh(I) occurs.

137 (a) Abel, E. W.; Moorhouse, S. *Angew. Chem. Int. Ed*. **1971**, *10*, 339-340. (b) Abel, E. W.; Moorhouse, S. *J. Chem. Soc. Dalton Trans*. **1973**, 1706-1711.

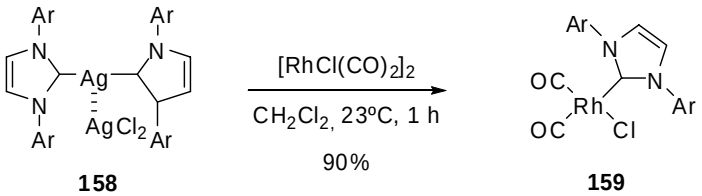
138 Nixon, J. F.; Poland, J. S.; Wilkins, B. *J. Organomet. Chem*. **1975**, *92*, 393-398.

139 For examples of β-oxygen elimination with Rh(I)-complexes see: (a) Miura, T.; Sasaki, T.; Nakazawa, H.; Murakami, M. *J. Am. Chem. Soc*. **2005**, *127*, 1390-1391. (b) Miura, T.; Sasaki, T.; Harumashi, T.; Murakami, M. *J. Am. Chem. Soc*. **2006**, *128*, 2516-2517.



Scheme 81

If the first step is the transmetalation such as we proposed, a catalyst of type *cis*-[RhCl(CO)$_2$(L)] should be a suitable candidate for the reaction since it contains π-acceptor ligands, which make it electron deficient, and a chloride atom that can bind to tin to promote the transmetalation. According to this argument, complex **159** was prepared following a described procedure for the synthesis of similar rhodium carbene complexes (Scheme 82).[140]



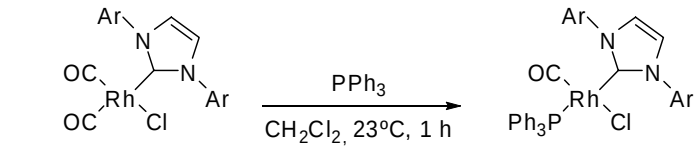
Scheme 82

Unfortunately, complex **159** resulted inactive as a catalyst. One of the carbonyl ligands in **159** was replaced by PPh_3 to formed complex **160** (Scheme 83).[141] This

140 (a) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663-1667. (b) Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem*. **2002**, 219-224.

141 Chen, A.; Ren, L.; Decken, A.; Crudden, C. *Organometallics* **2000**, *19*, 3459-3461.

complex also proved to be a poor catalyst leading to 20% of conversion after stirring in toluene at reflux for 12 h.

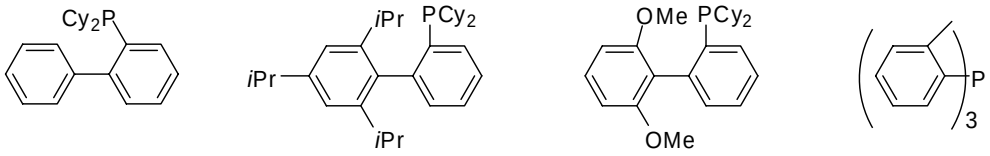


159 65% **160**

Ar = 2,4,6-trimethylbenzene

Scheme 83

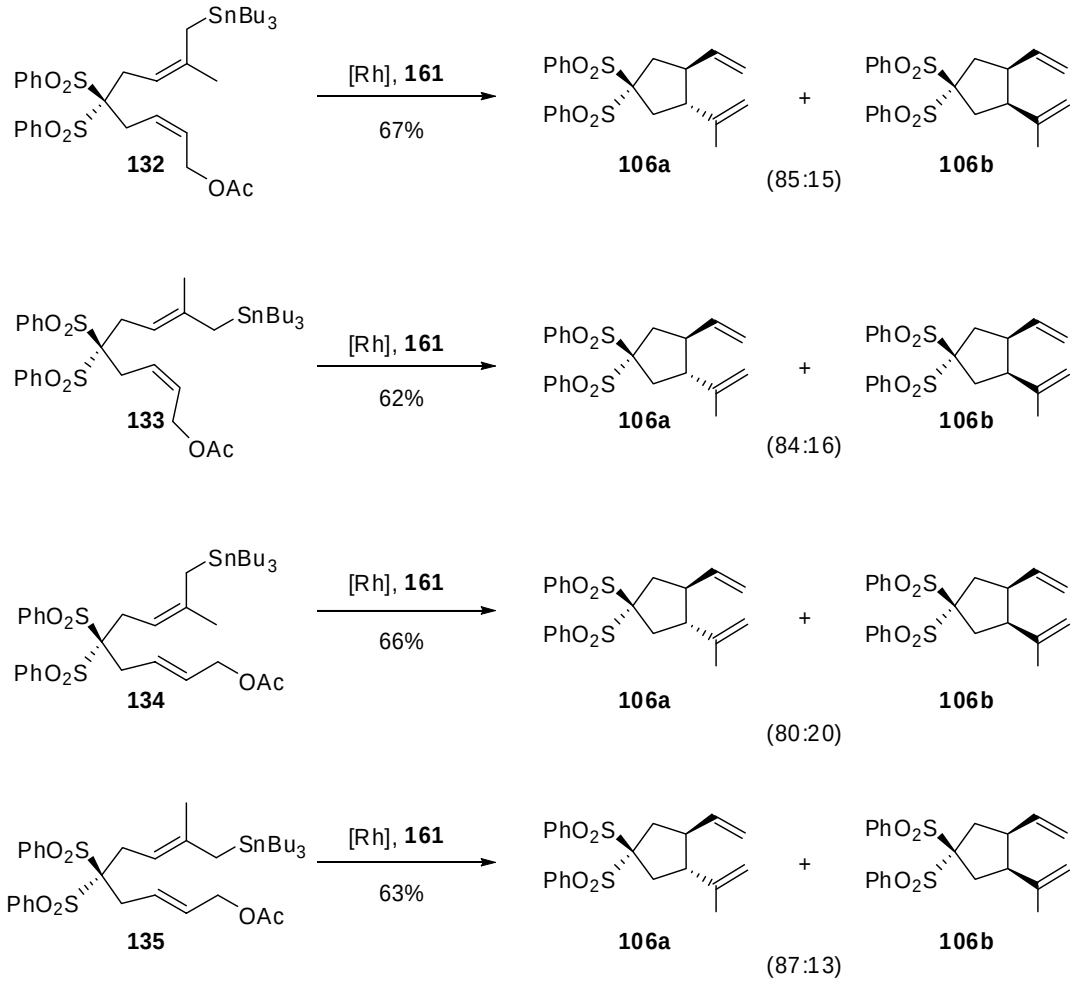
A new series of experiments were performed in order to examine the catalytic activity of $[RhCl(CO)_2]_2$ in the presence of different phosphines for the cyclization of substrates **132-135**. Along with the bidentate phosphines dppe, dppp, and dppf, were also essayed the bulky monodentade phosphines depicted in Figure 7. Among the bidentade phosphines tested, dppp, showed the highest activity leading to 50% of conversion, whereas the other gave lower conversions (26-31%). For the bulky phosphines, the better results were obtained for phosphines **161** and **162**, which led to complete conversion after 3 h, while **163**, and **164** led only to 69% and 77% of conversion, respectively. Addition of 3 equiv of *i*-Pr_2NH, Et_3N, or *i*-Pr_2NEt, reduced the amount of destannylated product formed, however increased the reactions times.



161 **162** **163** **164**

Figure 7

In Scheme 84 the results of the carbocyclization reaction with $[RhCl(CO)_2]_2$ for substrates **132-135** under the best reactions condition found for this catalyst, are summarized. Along with the carbocycles obtained within 62-67% yield, the product of destannylation was obtained in 7-12% yield in all cases. Substrates **134** and **135**, led to conversion values of 84 and 76%, respectively. The diastereoselectivities were of the same order as the ones obtained with $[RhCl(PPh_3)_3]$.



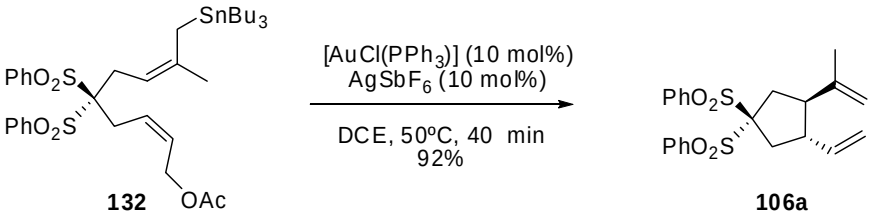
Scheme 84. [Rh] = $[Rh(CO)_2Cl]_2$ (5 mol%), **161** (10 mol%), *i*-Pr_2NH (3 equiv), toluene, 80ºC, 14 h.

No cyclization was observed with substrates **94**, **151** and **152**, which are the precursors of six-membered ring carbocycles, using $[RhCl(CO)_2]_2$ under all the conditions examined.

3. Gold-catalyzed cyclizations of allylstannnes with allylacetates

As rhodium(I) complexes proved to be less active catalysts than palladium(0) for these reactions, other metals were screened for the catalysis. We turned our attention to Ru(II) catalysts such as: $[RuClCp(PPh_3)_2]$, $[RuClCp(PPh_3)_2]/AgSbF_6$, and $[RuCl_2(CO)_2(PPh_3)_2]$ without success.

Although there are only a few examples of gold activation of alkenes (see Introduction, section 3), we decided to test gold(I) catalyst in the cyclization of allylstannanes with allylacetates. Unexpectedly, it was found that the cyclization takes place very efficiently to give only one diastereoisomer under the conditions depicted in Scheme 85.



Scheme 85

The results with different catalysts are summarized in Table 5. Remarkably, reaction of **132** with the cationic gold(I) complex **165**[142] (3 mol%) gave **106a** in 15 minutes (Table 5, entry 2). On the contrary, cationic silver(I) complex **166**[143] led to **106a** in only 44% yield together with a 19% of product of destannylation **168** at 80ºC (Table 5, entry 3). Reaction with a more electrophilic Au(I) catalyst formed from complex **167**[144] gave only the product of destannylation **169** (Table 5, entry 4), while a less electrophilic Au(I) complex formed from **170**[142] was not effective and led only to unchanged starting material (Table 5, entry 5). The cyclization of **132** could also be carried out at room temperature with cationic gold(I) complex **165** which highlights the mildness of this method compared to rhodium and palladium catalysis (entry 6).

Table 5. Screening of catalysts for the gold catalyzed cyclization.[a]

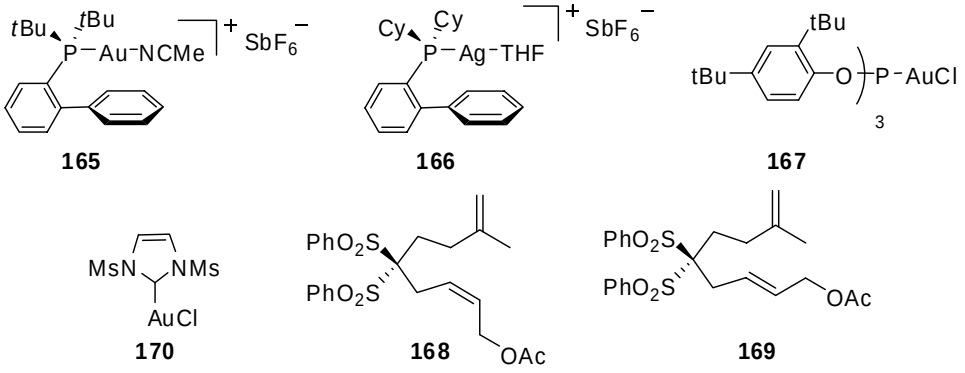
Entry	Substrate	Catalyst (mol%)	T(ºC)	t (h)	Product(s)	Yield (%)
1	**132**	[AuCl(PPh$_3$)] (10) AgSbF$_6$ (10)	50	0.6	**106a**	92
2	**132**	**165** (3)	50	0.25	**106a**	95
3[b]	**132**	**166** (10)	80	7	**106a** **168**	44 19
4	**134**	**167** (5) AgSbF$_6$ (5)	80	8	**169**	48
5	**134**	**170** (5) AgSbF$_6$ (5)	80	22	-	-
6	**132**	**165** (3)	23	14	**106a**	88

(a) All reactions were performed in DCE. (b) Conversion = 66%.

142 Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc*. **2005**, *127*, 6178-6179.

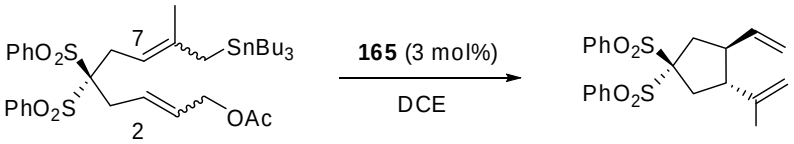
143 Porcel, S.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2007**, *46*, 2672-2676.

144 López, S.; Herrrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2006**, *45*, 6029-6032.



Similar to the reactions with Rh(I) complexes, the influence on the reactivity of the alkene configuration was examined with the different stereodefined compounds **132-135** (Table 6).

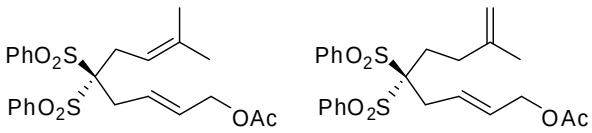
Table 6. Cyclization of **132-135** with cationic gold(I) complex **165**.



132: 2*Z*, 7*Z* **134:** 2*E*, 7*Z*
133: 2*Z*, 7*E* **135:** 2*E*, 7*E*

Entry	Substrate	T (ºC)	t (h)	Product(s)	Yield (%) (ratio)
1	**132**	50	0.25	**106a**	95
2	**133**	50	1.25	**106a**	92
3	**134**	80	19	**106a/106b** **171a/171b**	47 (56:45) 17 (1:1)
4[a]	**135**	80	19	**104a/104b** **171a/171b**	40 (56:45) 18 (1:1)

(a) conversión = 89%



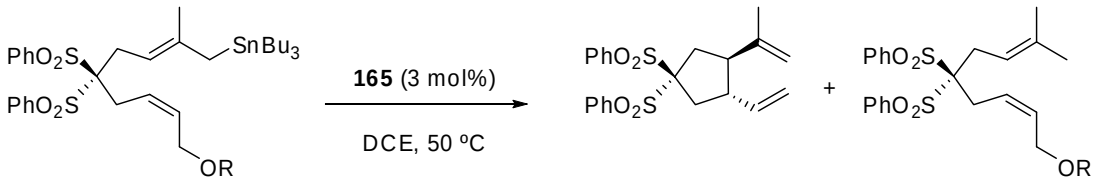
Similar to the results obtained with Rh(I) complexes, those substrates bearing an allyl acetate moiety with a *Z* configuration (Table 6, entries 1 and 2) were more reactive

than those with an *E* configuration (Table 6, entries 3 and 4). The least reactive substrate was **135** for which the conversion was only 89% after heating at 80ºC for 19 h. (Table 6, entry 4). It is noteworthy that while carbocycle **106** was obtained as a single diastereoisomer from substrates **132** and **133**, it was obtained as a mixture of *trans*/*cis* isomers in the case of **134** and **135**. In addition, a 1:1 regioisomeric mixture of destannylation products **171a** and **171b** was obtained with **133** and **135** in 17% and 18% yield, respectively (Table 6, entries 3 and 4).

Encouraged by the good results obtained with this catalytic system, we studied the generality of the reaction with different substrates.

3.1. Scope and limitations of the gold(I)-catalyzed allyl/allyl coupling

First, we studied the effect of varying the acetate by other functional groups. For this purpose, we synthesized compound **172** with a free OH, and substrates **174** and **175** with and ethyl carbonate and a trichoroethyl carbonate, respectively (Scheme 86). The reaction could be run out with the free allyl alcohol **172**, to give the carbocycle **106a** in 63% yield along with 27% of destannylated starting material (**173**). Reaction of ethyl carbonate **174** proceeded more sluggishly than its TROC analogue **175**, although in both cases the carbocycle was isolated in good yield.



172: R = H	1 h	**106a** (63%)	**173** (27%)
174: R = OCO_2Et	8 h	**106a** (88%)	-
175: R= $OCO_2CH_2CCl_3$	1 h	**106a** (95%)	-

Scheme 86

Reaction of substrates **176** and **177** (Figure 8) was also tested, although only partial destannylation of starting material was observed.

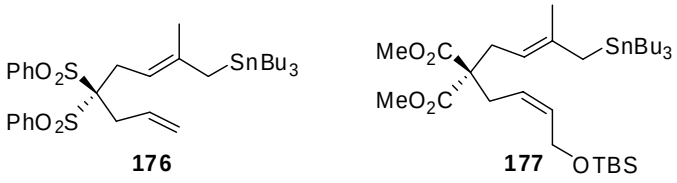
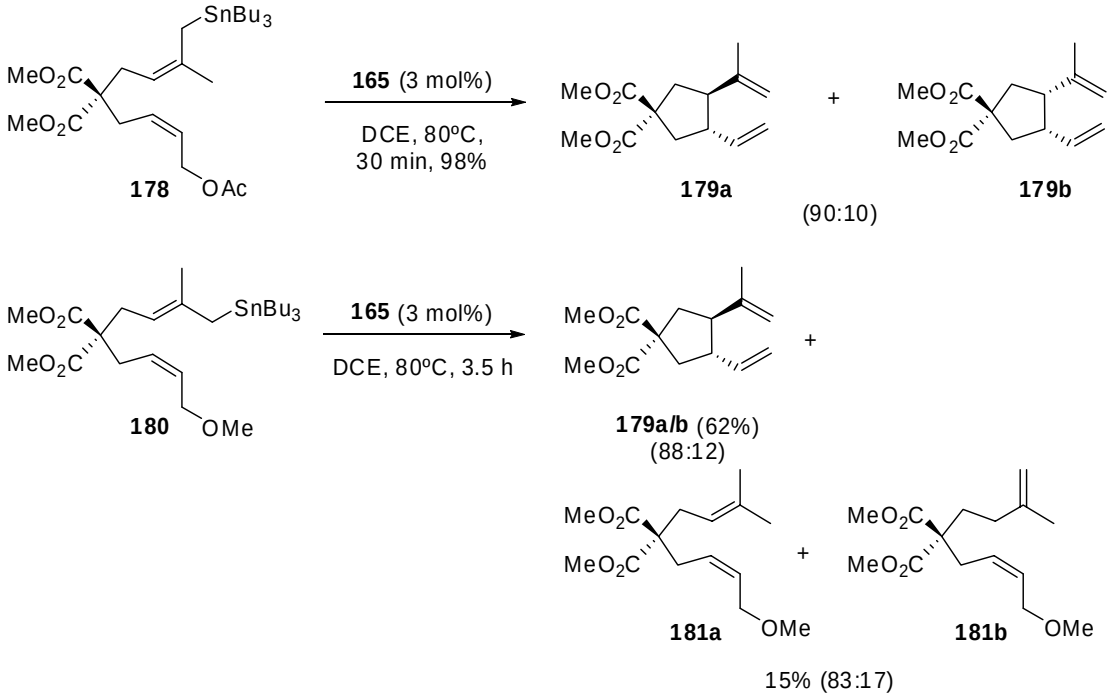


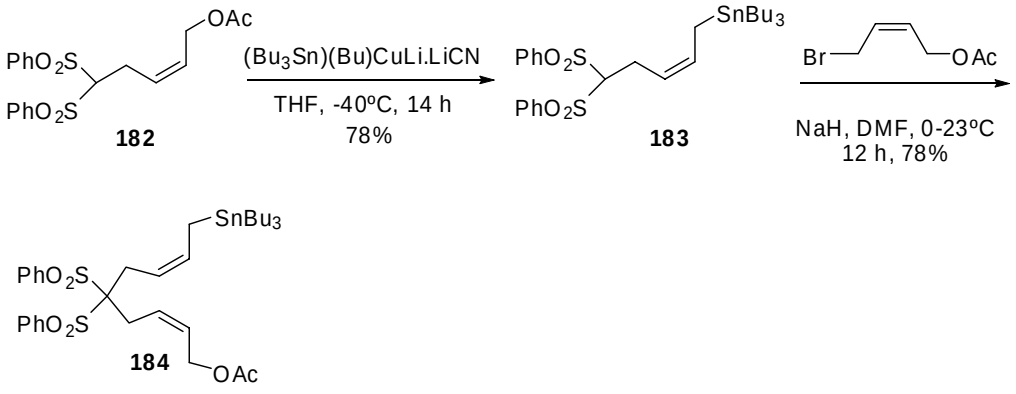
Figure 8

Next, we synthesized compounds **178** and **180** with a malonate at the tether and subjected them to the standard reaction conditions (Scheme 87). Both substrates gave the desired product **179**, although the reactions required higher temperatures than for sulfones. As expected, **180** with an allyl methyl ether was less reactive than its allyl acetate analogue **178**, and additionally gave a mixture of destannylated compounds **181a** and **181b**.



Scheme 87

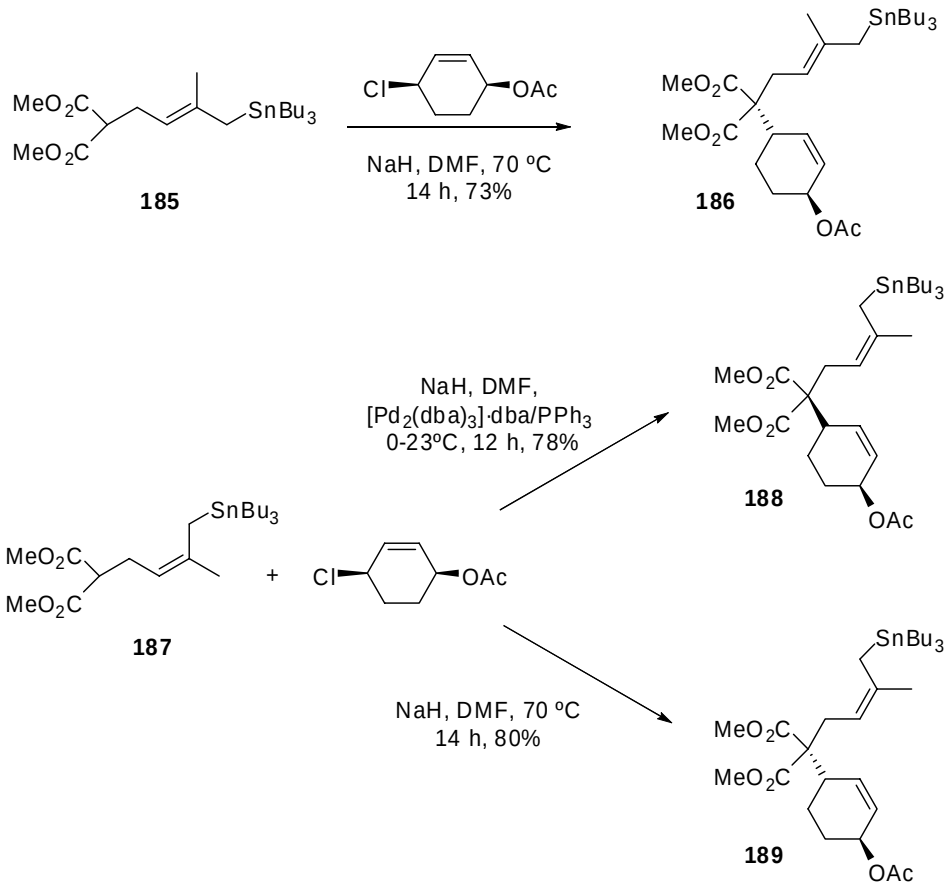
Compound **184**, in which both allyl moieties have disubstituted alkenes was synthesized from acetate **182**[145] as shown in Scheme 88.



Scheme 88

145 Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222.

The synthesis of **186** with a cyclohexane ring was performed by alkylation of allylstannane **185** with *cis*-1-acetoxy-4-chloro-2-cyclohexene[146] (Scheme 89). Substrates **188** and **189** were prepared from stannane **187**. To achieve a *cis* configuration between the acetate and the alkyl chain in **188**, the nucleophilic substitution was carried out with Pd(0) catalyst (Scheme 89).[146]

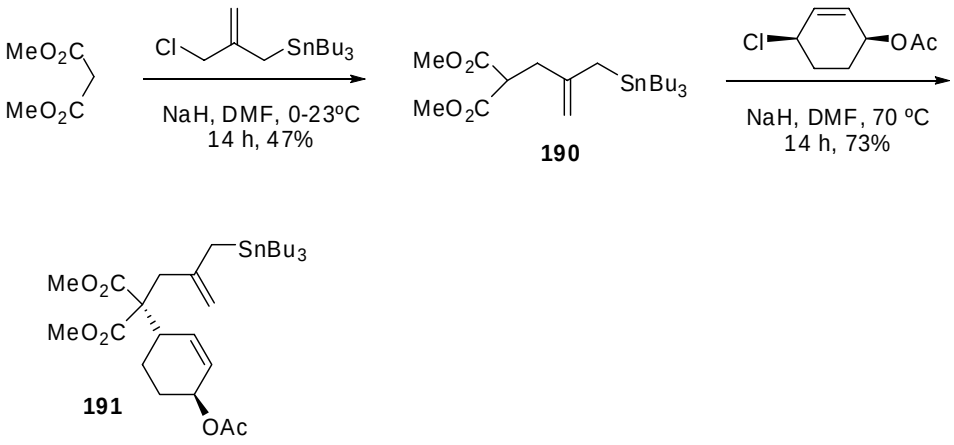


Scheme 89

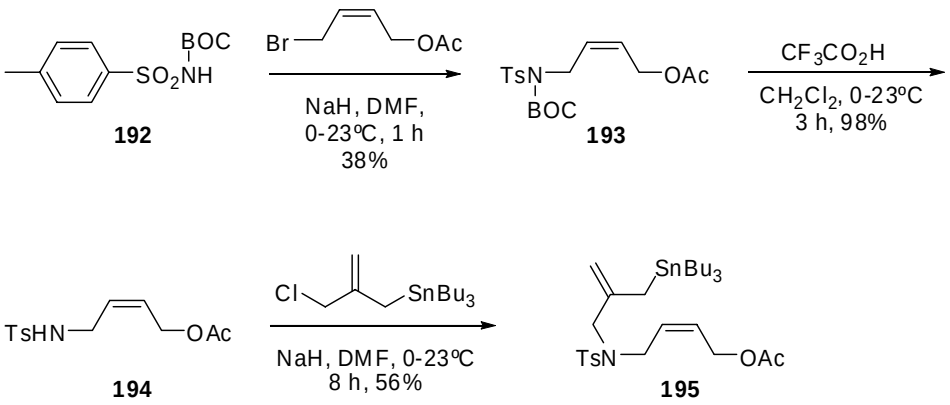
Product **191** with a methallylstannane was prepared from **190** by alkylation with *cis*-1-acetoxy-4-chloro-2-cyclohexene (Scheme 90). Compound **195** with an amide at the tether was synthesized from sulfonamide **192** (Scheme 91). Alkylation of **192** with (*Z*)-1-acetoxy-4-bromo-2-butene afforded **193**, which after treatment with trifluoroacetic acid gave **194**. The allylstannane moiety was introduced by alkylation of **194** with 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene.[147]

146 Bäckvall, J.-E.; Nyström, J.-E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *105*, 3676- 3686.

147 Keck, G. E.; Yu, T.; McLaws, M. D. *J. Org. Chem*. **2005**, *70*, 2543-2550.

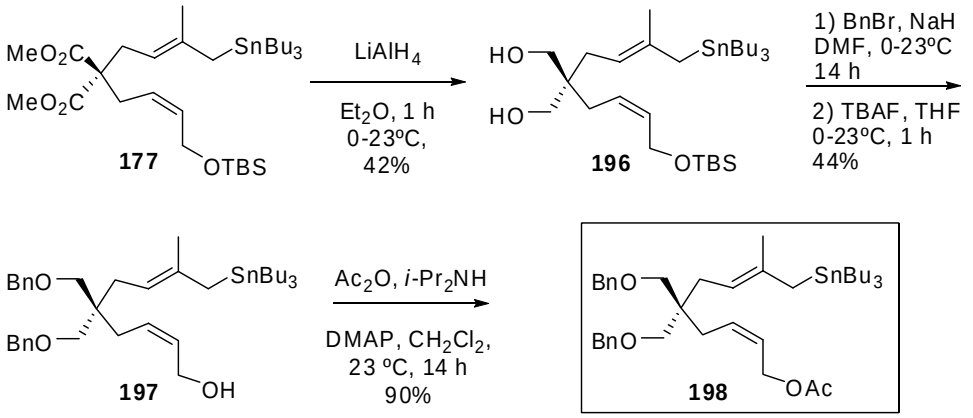


Scheme 90



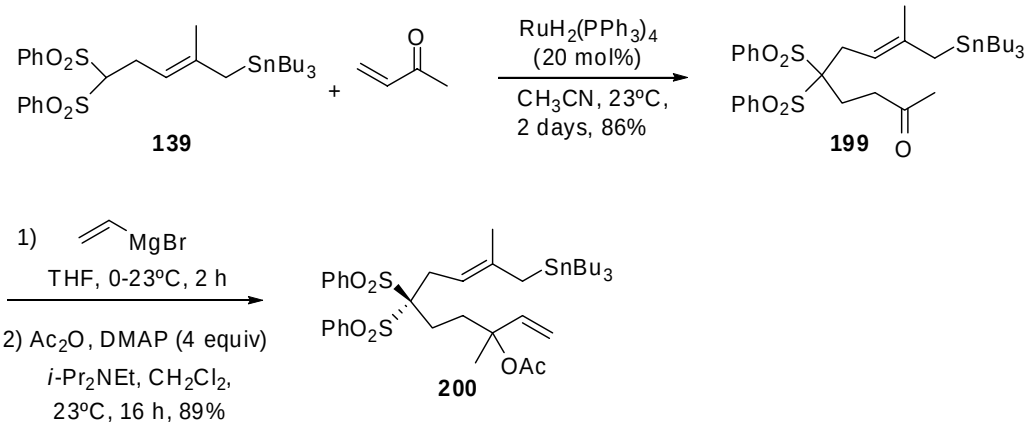
Scheme 91

We also synthesized allylstannane-allylacetate **198** to study the compatibility of the method with oxygen functionalities. We started from TBS-protected alcohol **177**, which was reduced with $LiAlH_4$ to give the diol **196** obtained in a 42% yield. Benzylation and cleavage of the TBS group afforded allyl alcohol **197** in a 44% yield. Acetylation of the free alcohol afforded compound **198** (Scheme 92).



Scheme 92

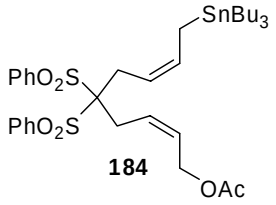
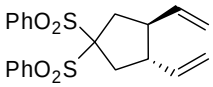
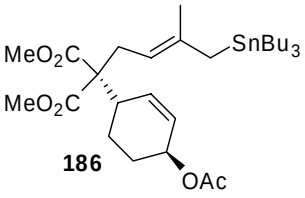
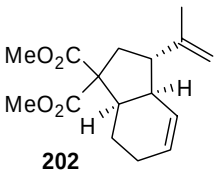
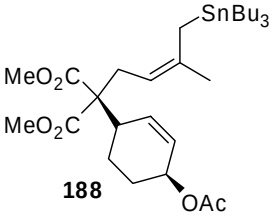
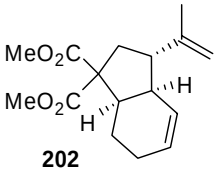
Finally, we synthesized compound **200** following a synthetic pathway previously described for this compound[107] (Scheme 93).

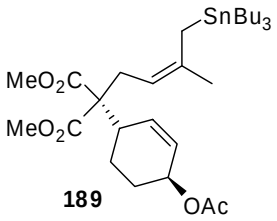
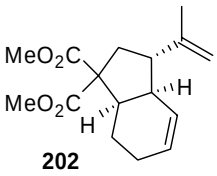
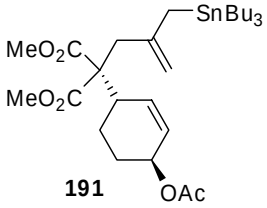
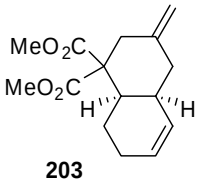
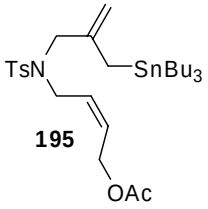
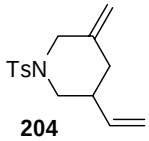
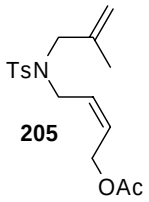
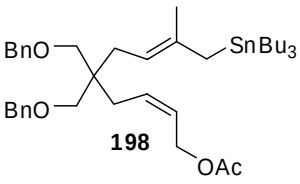
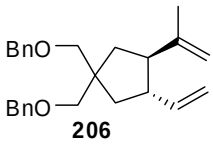


Scheme 93

In Table 7 the results of the cyclization reaction with these substrates under the optimized reaction conditions are summarized.

Table 7. Gold-catalyzed allylstannane-allylacetate cyclizations.

Entry[a]	Substrate	T(ºC)	t(h)	Product(s)	Yield
1	 **184**	80	1	 **201** (*t*/*c* 87:13)	86
2	 **186**	50	0.5	 **202**	94
3	 **188**	50	0.5	 **202**	99

Entry[a]	Substrate	T(ºC)	t(h)	Product(s)	Yield
4	 **189**	50	0.5	 **202**	94
5[b]	 **191**	80	0.5	 **203**	90
6	 **195**	80	1	 **204**  **205**	41 59
7	 **198**	80	0.5	 **206**	96

(a) 3 mol% of **165** in DCE. (b) 5 mol% of **165**.

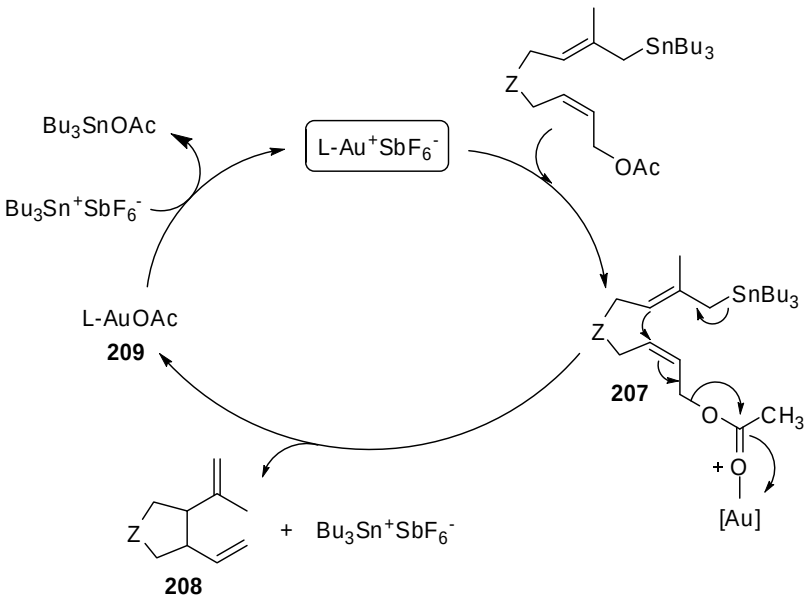
Substrate **184** with a less electron-rich olefin at the allylstannane moiety was less reactive than the analogues compound **132** (Table 6, entry 1) and needed 1 h at 80ºC to afford the carbocycle **201** with a slightly diminished yield (86%) (Table 7, entry 1). Interestingly, the cyclizations of **186**, **188** and **189** took place with complete stereoselectivity and good yields to afford *cis*-hydrindane **202** (Table 7, entries 2-4). It is important to note that the diastereoisomer obtained was always the same, independently of the relative configuration between the acetate and the alkyl chain in the cyclohexane ring and of the configuration at the allylstannane moiety. Excellent yield and stereoselectivity was also obtained in the cyclization of **191** (Table 7, entry 5), which gave the *cis*-decaline **203** as a single stereoisomer. Tosylamide **195** resulted less reactive and afforded piperidine **204** in only 41% yield along with 59% of the product

of destannylation **205** (entry 6). The cyclization of **198** showed that the method is compatible with benzylether functionalities as carbocycle **206** was obtained in 96% yield (entry 7).

Unfortunately, gold(I) also failed in the cyclization of substrates precursors of the six-membered skeletal of lobane diterpenes such as **94** and **200**. We essayed without success the cationic gold(I) complex **165**, **170** and **167** (in these last two cases in the presence of $AgSbF_6$).

3.2. Mechanistic proposal for the gold catalyzed cyclization

Although the mechanism of this allyl-allyl coupling is still not known, an oxidative addition of the allyl acetate to Au(I) seems rather unlikely.[148] We propose two reasonable mechanistic pathways for this process. In the first, gold(I) acts as a Lewis acid coordinating to the acetate and promoting the nucleophilic attack of the allylstannane in a S_N2' reaction (Scheme 94). This would lead to the cyclized compound (**208**) along with LAuOAc complex (**209**) that would react with tributytin hexafluoroantimoniate to regenerate the initial complex.

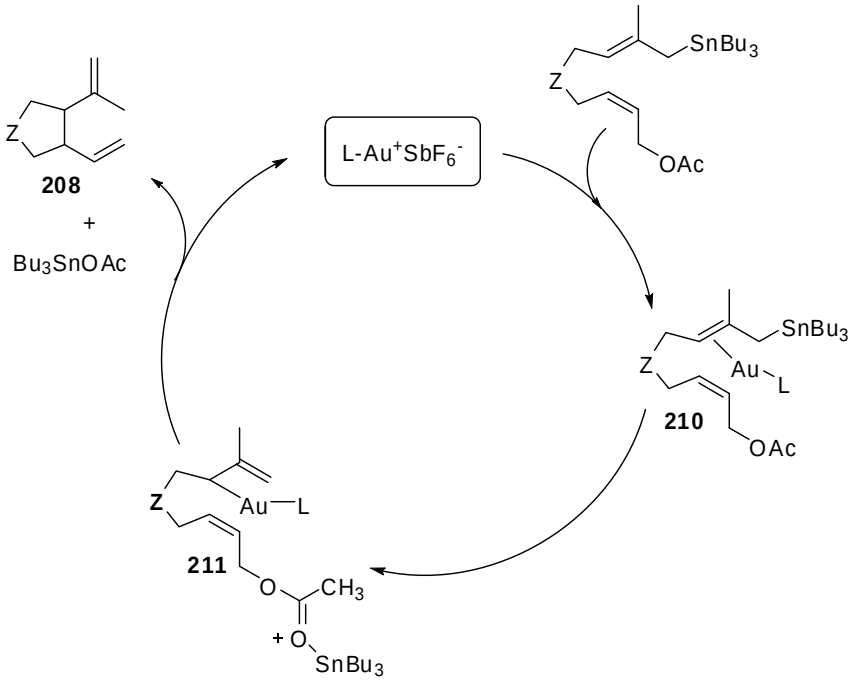


Scheme 94

148 (a) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed*. **2007**, *46*, 3410-3449. (b) Gorin, D. J.; Toste, F. D. Nature **2007**, *446*, 395-403. (c) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun*. **2006**, 333-346.

Precedents of intermolecular allyl coupling reactions of allylstannanes with allylic acetates promoted by a Lewis acid were described in 1985 by Sakurai et al., but stoichiometric amounts of the Lewis acid were required to perform the coupling.[149]

In the second pathway, gold coordinates to the more electron rich olefin of the substrate, the allylstannane, promoting the cleavage of the C-Sn bond to give an allylgold(I) intermediate **210** (Scheme 95). Nucleophilic attack of the allylgold(I) to the allyl acetate affords **211**. The S_N2'process could be facilitated by activation of the tributyltin cation generated in the first step.

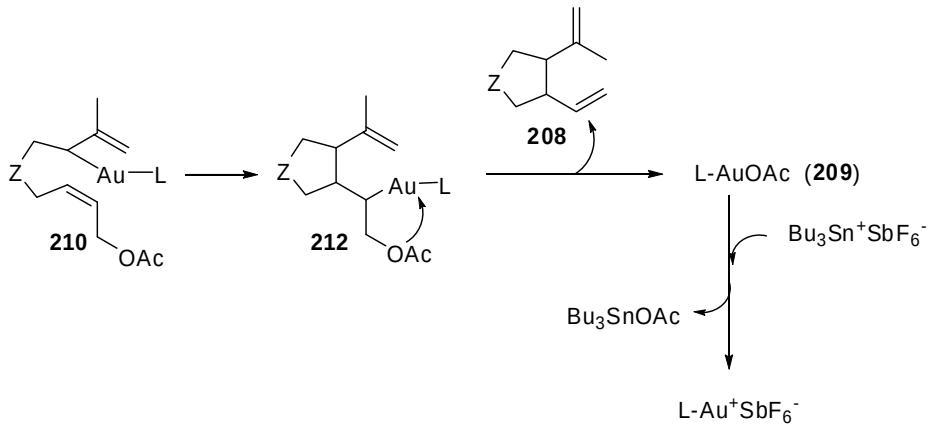


Scheme 95

Allylgold(I) complexes are not known, although a few allylgold(III) complexes have been prepared and have been shown to react with carbonyl compounds as nucleophiles at the γ carbon.[150]Alternatively, once the allylgold(I) is generated, it could undergo a 1,2-insertion into the olefin to give and alkenylgold(I) species (**212**) that would suffer β-acetate elimination to afford **208**. Again, complex **209** could react with tributytin hexafluoroantimoniate to regenerate the initial gold(I) complex (Scheme 96).

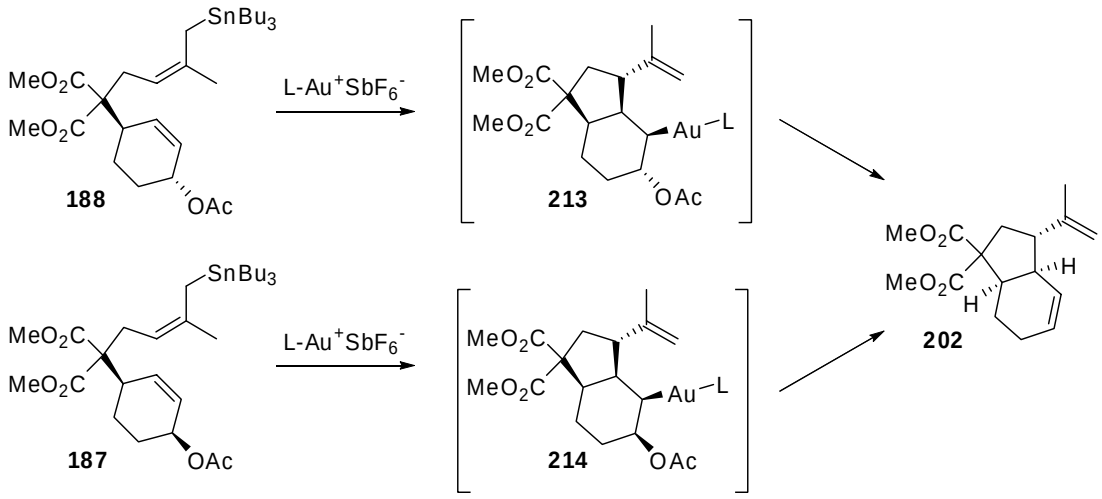
149 Hosomi, A.; Imai, T.; Endo, M.; Sakurai, H. *J. Organomet. Chem*. **1985**, *285*, 95-107.

150 Sone, T.; Ozaki, S.; Kasuga, N. C.; Fukuoka, A.; Komiya, S. *Bull. Chem. Soc. Jpn*. **1995**, *68*, 1532-1533.



Scheme 96

This last option is unlikely as β-elimination processes have geometric restrictions that would result in significant differences between substrates **187** and **188**. Thus, after the insertion step, elimination from intermediates **213** and **214** would take place with very different ratio and/or efficiencies (Scheme 97).



Scheme 97

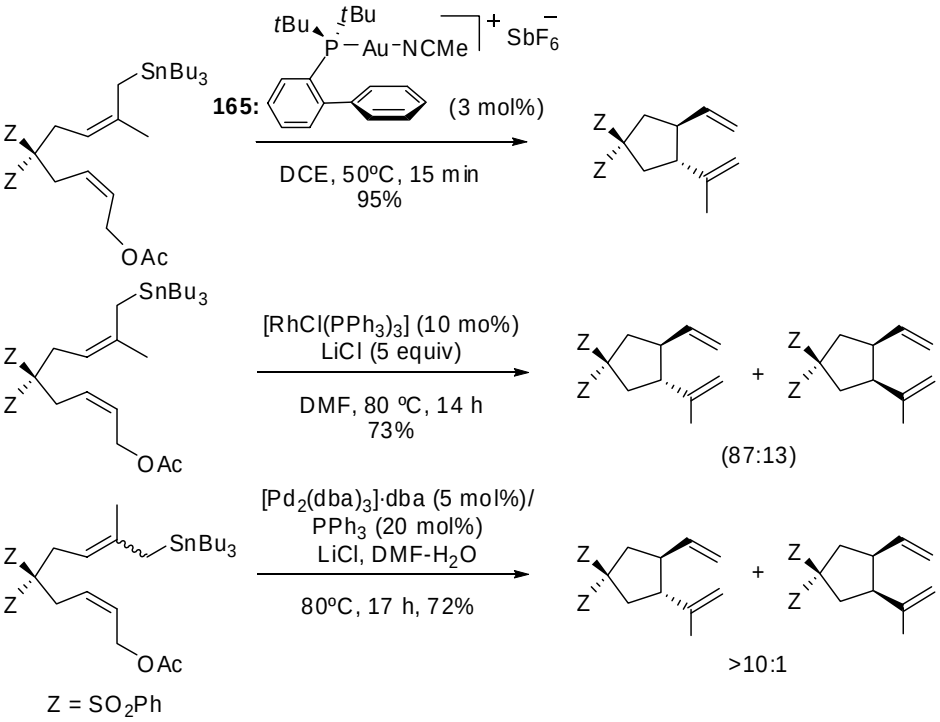
Further investigations to elucidate the mechanistic pathway of the reaction are being carried out in our group at the moment

Chapter 1. Conclusions

Conclusions

The intramolecular reaction of allylstannanes with allylacetates can be catalyzed not only by Pd(0) but also by Rh(I) and Au(I) complexes. In the case of Rh(I) and Au(I), differences on reactivity were found depending on the olefinic geometry of the substrate. The more reactive substrates were those in which the allyl acetate moiety has a *Z* configuration.

Preferential formation of *trans*-five membered ring compounds was showed with both Rh(I) and Au(I) catalysts, similar to the stereoselectivity displayed by Pd(0). Remarkably, the most active catalytic system for the cyclization was the cationic gold(I) complex (**165**) as depicted in Scheme 98.



Scheme 98

The formation of the six-membered ring carbocycles which are the precursors for lobane diterpenes, failed. It is however noteworthy that the reactivity displayed by Rh(I) and Au(I) in these transformations has never been observed before. This is more prominent in the case of Au(I), not only because there are only a few examples in which gold activate alkenes (see Introduction section 3) but also because the results obtained in these cyclizations with gold(I) outperformed all other catalysts.

The reaction catalyzed by Rh(I) presumably proceeds via transmetalation with the stannane, insertion of the resulting (η^3-allyl)rhodium complex into the alkene and β-elimination of Rh-OAc. The reaction catalyzed by Au(I) may proceed through transmetalation with the allylstannane, to form an allylgold(I) intermediate which attacks the olefin as a nucleophile, or via activation of the acetate by simple coordination of gold(I) as Lewis acid and attack of the stannane onto the olefin.

Chapter 1. Experimental Section

Experimental section: Index

Methods and Materials:

400 MHz ^{1}HMR, 100 MHz ^{13}C NMR, and 162 MHz ^{31}P NMR spectra were recorded at 23 ºC on a Bruker Avance 400 Ultrashield. Mass Spectrometry was performed on Waters LCT Premier (ESI) and Waters GCT (EI, CI) spectrometers. Infrared spectra were recorded on a Bruker Tensor 27 equipped with MKII Golden Gate Specac Single reflection ATR system. Melting points were determined using a Büchi-B450 apparatus. Thin layer chromatography was carried out using TCL-Aluminium sheets with 0.2 mm of silica gel (Merk GF_{234}). Column chromatography purifications were performed using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 μm).

All reactions and manipulations were performed under Ar or N_2 in standard laboratory glassware. Solvents were dried using a Solvent Purification System (SPS). Extractive workup refers to partitioning of the crude reaction between an organic solvent and water, phase separation, drying (Na_2SO_4 or $MgSO_4$), and evaporation under reduced pressure. The saturated aqueous NH_4Cl solution was adjusted to pH = 8 by addition of NH_4OH.

Catalysts:

The following complexes were prepared according to described procedures: $[Pd_2(dba)_3]\cdot dba$,[151] $[PdCl_2(MeCN)_2]$,[152] $[Pd(MeCN)_2](BF_4)_2$,[153] $[RhCl(cod)]_2$,[133] $[Rh(cod)_2]BF_4$,[134] $[RhCl(CO)(PPh_3)_2]$,[136] $[RuClCp(PPh_3)_2]$,[154] $[RuCl_2(CO)_2(PPh_3)_2]$,[136] and $[Au\{P[C_6H_4(o\text{-}Ph)](t\text{Bu})_2\}(NCMe)]SbF_6$.[155] The complexes $[RhCl(PPh_3)_3]$ (Aldrich), and $[RhCl(CO)_2]_2$ (Strem) were used as received.

151 Takahashi, Y.; Ito, Ts.; Sakai, S.; Ishii, Y. *Chem. Commun*. **1970**, *17*, 1065-1066.

152 Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: London, **1985**, p. 17.

153 (a) Tomas, R. R.; Sen, A. *Inorg. Synth*. **1989**, *26*, 128. (b) Tomas, R. R.; Sen, A. *Inorg. Synth*. **1990**, *28*, 63.

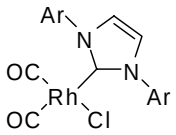
154 Bruce, M. I.; Hameister, C.; Swincer, A. G.; Wallis, R. C. *Inorg. Synth*. **1982**, *21*, 78.

155 Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2006**, *45*, 5455-5459.

[Rh(cod)(dppf)]BF_4 (153).

This complex was synthesized according to a reported procedure for a related cationic Rh(I) complex.[135] A solution of dppf (100 mg, 0.25 mmol) in THF (5 mL) was added dropwise to a solution of $[Rh(cod)_2]BF_4$ in MeOH (10 mL) at 23ºC. The reaction was stirred for 1 h, the solvent was evaporated and the orange solid which was obtained was washed with Et_2O (3 x 3 mL) to yield **153** (165 mg, 78%). This solid was recrystallized from dichlorometane/pentane; m.p. (dec.) > 210 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.76 (m, 8H), 7.68-7.50 (m, 12H), 4.42 (bs, 4H), 4.34 (bs, 4H), 4.28 (bs, 4H), 2.47-2.33 (m, 4H), 2.24-2.08 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.15 (t, $J(^{13}C\text{-}^{31}P)$ = 5. 8Hz), 131.80 (s), 131.83 (overlapping dd, $J(^{13}C\text{-}^{31}P)$ = 54.1, $J(^{13}C\text{-}^{103}Rh)$ = 10.4 Hz), 129.14 (t, $J(^{13}C\text{-}^{31}P)$ = 5. 1 Hz), 99.35 (m), 75.04 (t, $J(^{13}C\text{-}^{31}P)$ = 5. 8 Hz), 74.14 (t, $J(^{13}C\text{-}^{31}P)$ = 3. 6 Hz), 72.79 (m), 30.50 (s). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.08 (d, . $J(^{31}P\text{-}^{103}Rh)$ = 148.6 Hz). HRMS-ESI Cald for $C_{42}H_{40}FeRhP_2$ $[M]^+$: 765.1010. Found: 765.1017.

Complex 159.[140]



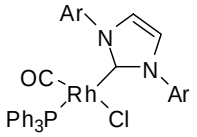
Ar = 2,4,6-trimethylbenzene

Compound **158**[140] (50 mg, 0.05 mmol) and $[RhCl(CO)_2]_2$ (22 mg, 0.05 mmol) were dissolved in CH_2Cl_2 (2.5 mL), the mixture was stirred at 23ºC for 1 h and then filtered over Celite. The solution was concentrated under vacuum and the resulting yellow powder was washed with pentane (3 x 2 mL) to give **159** (22 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (s, 2H), 7.01 (s, 4H), 2.37 (s, 6H), 2.22 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.89 (d; $J(^{13}C\text{-}^{103}Rh)$ = 54.0 Hz), 182.77 (d; $J(^{13}C\text{-}^{103}Rh)$ = 74.5 Hz), 177.60 (d; $J(^{13}C\text{-}^{103}Rh)$ = 44.9 Hz), 139.37, 135.27, 135.12, 129.29, 123.71, 21.19, 18.47. FT-ATR: υ(CO) 2070, 1985 cm^{-1} (similar intensities). HRMS-ESI Cald for $C_{23}H_{24}N_2O_2Rh$ $[M\text{-}HCl]^+$: 463.0893. Found: 463.0914.

135 Hoge, Garrett; Wu, H.-P.; Kissel, W. S.; Pflum, D. A.; Greene, D. J.; Bao, J. *J. Am. Chem. Soc*. **2004**, *126*, 5966-5967.

140 (a) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663-1667. (b) Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem*. **2002**, 219-224.

Complex 160.[141]



Ar = 2,4,6-trimethylbenzene

Complex **159** (40 mg, 0.08 mmol), and PPh_3 (21 mg, 0.08 mmol), were dissolved in CH_2Cl_2 (5 mL). Immediately gas evolution was observed. The reaction was stirred at 23ºC for 1 h after which the solvent was reduced to 1 mL. Addition of pentane afforded a yellow precipitate which was filtered off and washed with pentane (3 x 2 mL) to yield **160** (38 mg, 65%). This solid was recrystallized from dichlorometane/pentane. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.25 (m, 6H), 7.24-7.17 (m, 3H), 7.16-7.08 (m, 6H), 7.02 (s, 2H), 6.95 (s, 4H), 2.35 (s, 6H), 2.20 (bs, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.02 (dd; $J(^{13}C\text{-}^{103}Rh)$ = 77.9, $(^{13}C\text{-}^{31}P)$ = 17.2 Hz), 184.14 (dd; $J(^{13}C\text{-}^{103}Rh)$ = 123.3, $(^{13}C\text{-}^{31}P)$ = 47.25 Hz), 138.30, (s), 136.36 (s), 136.01 (brs), 134.71 (d, $J(^{13}C\text{-}^{31}P)$ = 11.7 Hz), 134.36 (d, $J(^{13}C\text{-}^{31}P)$ = 40.92 Hz), 129.29 (d, $J(^{13}C\text{-}^{31}P)$ = 2.3 Hz), 128.96 (s), 127.57 (d, $J(^{13}C\text{-}^{31}P)$ = 9.5 Hz), 122.90 (d, $J(^{13}C\text{-}^{31}P)$ = 2.9 Hz), 21.28 (s), 18.94 (s). ^{31}P (162 MHz, $CDCl_3$) δ 35.34 (d, $J(^{31}P\text{-}^{103}Rh)$ = 115.0 Hz). FT-ATR: υ(CO) 1940 cm^{-1}. HRMS-ESI Cald for $C_{40}H_{39}N_2ORhP$ $[M\text{-}HCl]^+$: 697.1855. Found: 697.1840.

General procedures for preparation of allylstannane-allylacetates:

General procedure for nucleophilic opening of vinyl epoxides.

To a solution of starting material (5.0 mmol), $[Pd_2(dba)_3]$·dba (0.025 mmol), and dppe (0.5 mmol, 10 mol%) in THF (15 mL) at 23°C was added the corresponding vinyl epoxide (5.0 mmol). The resulting mixture was stirred at 23 °C until TLC showed full conversion, was filtered through a pad of Celite and concentred. Chromatography (hexane-EtOAc mixtures) afforded the corresponding allylic alcohols.

General acetylation procedure.

To a solution of alcohol (0.35 mmol), DMAP (0.035 mmol) and *i*-Pr_2NEt (0.42 mmol) in CH_2Cl_2 (5 mL) was added Ac_2O (0.39 mmol). The mixture was stirred at

141 Chen, A.; Ren, L.; Decken, A.; Crudden, C. *Organometallics* **2000**, *19*, 3459-3461.

23°C until TLC showed full conversion (2-23 h). After extractive workup (CH_2Cl_2) and chromatography (hexane-EtOAc), the corresponding acetates were obtained.

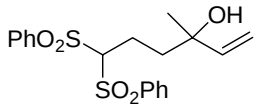
General procedure for the synthesis of allylstannanes from allyl acetates.[124]

To a suspension of CuCN (21 mmol) in THF (25 mL) at -78°C was added *n*-BuLi (2.5 M solution in hexane, 16.8 mL, 42 mmol). The mixture was stirred at -60°C for 3 h. The resulting pale yellow solution was cooled to -78 °C and *n*-Bu_3SnH (42 mmol) was slowly added to give a bright yellow solution. Thereafter, a solution of allylacetate (10 mmol) in THF (10 mL) was added and the reaction was stirred at -40 °C for 12 h. The reaction mixture was warmed to 23°C and quenched by addition of saturated aqueous NH_4Cl (pH = 8). After extractive workup (Et_2O/H_2O) and chromatography (hexane-EtOAc), the corresponding stannanes were obtained.

General procedure for alkylation with NaH

To a suspension of NaH (60% in mineral oil, 1.60 mmol) in DMF (10 mL) at 0ºC was added a solution of substrate (1.60 mmol) in DMF (5 mL). The mixture was stirred for 10 min, then the alkyl halide (1.60 mmol) was added. The reaction mixture was stirred at 23ºC for 16 h. After extractive work-up (Et_2O/H_2O/brine) and chromatography (hexane-EtOAc) the title compounds were obtained.

6,6-Bis(phenylsulfonyl)-3-methyl-1-hexen-3-ol (128).[107]



To a solution of 5,5-bis(phenylsulfonyl)-pentan-2-one[156] (5.1 g, 13.9 mmol) in THF (20 mL) was slowly added vinylmagnesium bromide (29.8 mL, 1 M in THF, 29.8 mmol) at 0 °C. The mixture was stirred at 23 °C for 2 h, after which the reaction was quenched by addition of water (5 mL). After the extractive workup (Et_2O/water) the residue was purified by column chromatography (1:1 hexane-EtOAc) to yield **128** as a white solid (4.62 g, 84%). ^1H NMR (400 MHZ, $CDCl_3$) δ 8.00-7.90 (m, 4H), 7.74-7.65

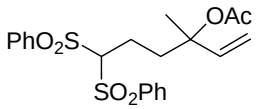
124 Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.* **1989**, *30*, 2065-2068.

107 Cuerva, J. M.; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. *J. Org. Chem.* **1997**, *62,* 7540-7541.

156 Gómez-Bengoa, E.; Cuerva, J. M. Mateo, C.; Echavarren, A. M. *J. Am. Chem. Soc*. **1996**, 118, 8553-8565.

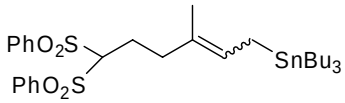
(m, 2H), 7.62-7.52 (m, 4H), 5.77 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.14 (d, *J* = 17.3 Hz, 1H), 5.04 (d, *J* = 10.8 Hz, 1H), 4.77 (t, *J* = 5.7 Hz, 1H), 2.34-2.16 (m, 2H), 1.97-1.77 (m, 2H), 1.60 (br s, 1H), 1.24 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 143.74, 137.91, 134.46, 129.59, 129.03, 112.73, 83.16, 73.20, 38.80, 28.44, 20.82. MS-ESI $[M+Na]^+$: 417.1.

3-Acetoxy-6,6-bis(phenylsulfonyl)-3-methyl-1-hexene (129).[107]



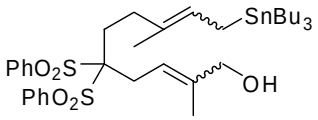
This compound was prepared from **128** following the general procedure for acetylation. After purification by column chromatography (2:1 to 1:1 hexane-EtOAc) a white solid was obtained (89%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.97-7.89 (m, 4H), 7.71-7.65 (m, 2H), 7.61-7.53 (m, 4H), 5.82 (dd, *J* = 17.8, 11.1 Hz, 1H), 5.12 (d, *J* = 11.3 Hz, 1H), 5.09 (d, *J* = 17.1 Hz, 1H), 4.39 (t, *J* = 5.5 Hz, 1H), 2.24-2.13 (m, 4H), 1.95 (s, 3H), 1.49 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 169.65, 140.57, 137.83, 134.61, 129.62, 129.60, 129.12, 114.14, 83.75, 82.08, 38.07, 23.75, 22.07, 20.38. MS-ESI $[M+Na]^+$: 459.1.

6,6-Bis(phenylsulfonyl)-3-methyl-1-(tri-*n*-butylstannyl)-2-hexene (130).[107]



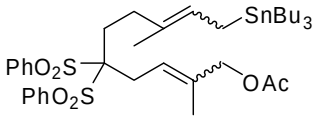
This compound was prepared from **129** following the general stannylation procedure. After purification by column chromatography (4:1 hexane-EtOAc), **130** was obtained as a vitreous solid (90%). Mixture of isomers (3:1): ^{1}H NMR (300 MHZ, $CDCl_3$) δ 8.03-7.93 (m, 4H, major and minor), 7.76-7.67 (m, 2H, major and minor), 7.64-7.54 (m, 4H, major and minor), 5.43 (t, *J* = 9.6 Hz, 1H, minor), 5.35 (t, *J* =9.6 Hz, 1H, major), 4.50 (t, *J* = 5.2 Hz, 1H, major), 4.45 (t, *J* = 4.9 Hz, 1H, minor), 2.36-2.62 (m, 4H, major and minor), 1.75-1.22 (m, 11H, major and minor), 0.99-0.72 (m, 15H, major and minor).

6,6-Bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadien-10-ol (131).[107]



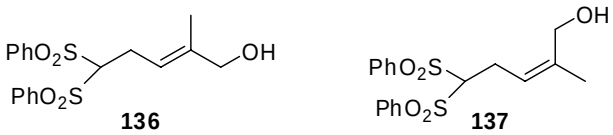
This compound was synthesized from **130** and 2-methyl-2-vinyloxirane following the general procedure for nucleophilic opening of vinyl epoxides. The crude mixture was purified by column chromatography (4:1 to 1:1 hexane-EtOAc) to afford **131** (93%) as a colorless oil (mixture of isomers): ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.18-8.01 (m, 4H, four isomers), 7.76-7.68 (m, 2H, four isomers), 7.65-7.54 (m, 4H, four isomers), 5.69 (t, *J* = 6.7 Hz, 1H, two isomers), 5.42 (t, *J* = 7.6 Hz, 1H, two isomers), 5.37 (t, *J* = 9.6 Hz, 1H, , four isomers), 4.14 (m, 1H, four isomers), 4.08-4.00 (m, 2H, four isomers), 3.15 (d, *J* = 7.0 Hz, 2H, one isomer), 3.12 (d, *J* = 7.0 Hz, 2H, one isomer), 3.07 (d, *J* = 6.1 Hz, 2H, one isomer), 3.03 (d, *J* = 6.1 Hz, 2H, one isomer), 2.30 (m, 4H, four isomers), 1.90-1.23 (m, 20H, four isomers), 0.98-0.73 (m, 15H, four isomers).

10-Acetoxy-6,6bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadiene (94).[107]



This compound was prepared from **131** following the general acetylation procedure. After purification by column chromatography (3:1 hexane-EtOAc), **94** was obtained as a colorless oil (89%, mixture of four isomers): ^{1}H NMR (200 MHZ, $CDCl_3$) δ 8.12-8.03 (m, 4H, four isomers), 7.76-7.67 (m, 2H, four isomers), 7.63-7.55 (m, 4H, four isomers), 5.74 (t, *J* = 4.5 Hz, 1H, two isomers), 5.63 (t, *J* = 4.9 Hz, 1H, two isomers), 5.40-5.29 (m, 1H, , four isomers), 4.58-4.45 (m, 2H, four isomers), 3.13 (d, *J* = 5.8 Hz, 2H, one isomer), 3.09 (d, *J* = 5.6 Hz, 2H, one isomer), 3.05 (d, *J* = 6.2 Hz, 2H, one isomer), 3.01 (d, *J* = 5.9 Hz, 2H, one isomer), 2.38-2.22 (m, 4H, four isomers), 2.11 (s, one isomer), 2.10 (s, one isomer), 2.08 (s, one isomer), 2.06 (s, one isomer), 1.84-1.24 (m, 20H, four isomers), 0.98-0.73 (m, 15H, four isomers).

(*E*)-5,5-Bis(phenylsulfonyl)-2-methyl-2-penten-1-ol (136);
(*Z*)-5,5-Bis(phenylsulfonyl) -2-methyl-2-penten-1-ol (137).[157]

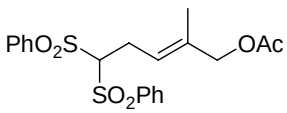


These compounds were prepared from bis(phenylsulfonlyl)methane and 2-methyl-2-vinyloxirane following the general procedure for nucleophilic opening of vinyl epoxides. They were obtained as mixture of regioisomers and were separated by column chromatography (4:1 to 2:1 hexane-EtOAc). The configuration was assigned by NOESY experiment.

136: Yield: 59%. White solid; m.p. 88-90 ºC. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.02-7.89 (m, 4H), 7.75-7.65 (m, 2H), 7.63-7.52 (m, 4H), 5.38 (t, *J* = 6.3 Hz, 1H), 4.47 (t, *J* = 6.1 Hz, 1H), 3.89 (d, *J* = 5.2 Hz, 2H), 2.93 (t, *J* = 6.3 Hz, 2H), 1.55 (s, 3H), 1.29 (t, *J* = 5.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.86, 138.03, 134.59, 129.51, 129.59, 129.10, 118.80, 83.74, 67.80, 24.28, 13.63. Anal. Calcd for $C_{18}H_{20}O_5S_2$: C, 56.82; H, 5.30; S, 16.86. Found: C, 56.61; H, 5.29; S, 16.72. MS-ESI $[M+Na]^+$: 403.0, $[M+K]^+$: 419.0.

137: Yield: 35%. White solid; m.p. 110-113 ºC. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.00-7.89 (m, 4H), 7.74-7.66 (m, 2H), 7.62-7.52 (m, 4H), 5.19 (t, *J* = 7.2 Hz, 1H), 5.86 (t, *J* = 5.7 Hz, 1H), 4.04 (s, 2H), 3.01 (t, *J* = 6.6 Hz, 2H), 1.81 (s, 1H), 1.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.11, 138.05, 134.60, 129.51, 129.11, 121.28, 83.99, 61.27, 24.31, 21.73. Anal. Calcd for $C_{18}H_{20}O_5S_2$: C, 56.82; H, 5.30; S, 16.86. Found: C, 56.16; H, 5.19; S, 16.72. MS-ESI $[M+Na]^+$:403.0, $[M+K]^+$: 419.0.

(*E*)-5,5-Bis(phenylsulfonyl)-2-methyl-2-penten acetate (138).[158]

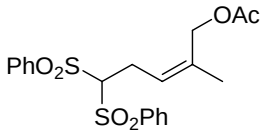


157 Described as mixture of *E*/*Z* isomers in: Fernández-Rivas, C.; Méndez, M.; Nieto-Overhuber, C.; Echavarren, A. M. *J. Org. Chem*. **2002**, *67*, 5197-5201.

158 Described as a *E*/*Z* isomers in: Cuerva, J. M; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. M. *J. Org. Chem*. **1997**, *62*, 7540-7541.

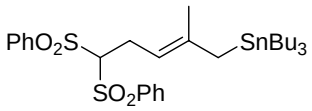
This compound was prepared from **136** following the general acetylation procedure. After purification by column chromatography (2:1 hexane-EtOAc), **138** was obtained as a white solid (79%); m.p. 80-82 ºC. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.02-7.91 (m, 4H), 7.76-7.66 (m, 2H), 7.64-7.53 (m, 4H), 5.42 (t, *J* = 6.7 Hz, 1H), 4.45 (t, *J* = 6.2 Hz, 1H), 4.35 (s, 2H), 2.94 (t, *J* = 6.5 Hz, 2H), 2.07 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.63, 137.95, 134.63, 134.20, 129.64, 129.11, 121.94, 83.68, 68.73, 24.32, 20.89, 13.91. MS-ESI $[M+Na]^+$: 445.1.

(*Z*)-5,5-Bis(phenylsulfonyl) -2-methyl-2-penten acetate (140).[158]



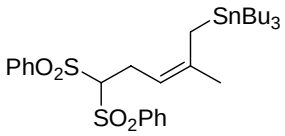
This compound was prepared from **137** following the general acetylation procedure. After purification by column chromatography (2:1 hexane-EtOAc), **140** was obtained as a white solid (79%); m.p. 79-81 ºC. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.00-7.90 (m, 4H), 7.74-7.65 (m, 2H), 7.62-7.53 (m, 4H), 5.39 (t, *J* = 7.2 Hz, 1H), 4.66 (t, *J* = 6.1 Hz, 1H), 4.44 (s, 2H), 2.99 (t, *J* = 6.7 Hz, 2H), 2.05 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.66, 138.05, 134.53, 134.32, 129.62, 129.05, 123.43, 83.46, 62.59, 24.08, 21.30, 20.83. Anal. Calcd for $C_{20}H_{22}O_6S_2$: C, 56.85; H, 5.25; S, 15.18. Found: C, 56.65; H, 5.17; S, 15.20. MS-ESI $[M+Na]^+$: 445.1.

(*E*)-5,5-Bis(phenylsulfonyl)-2-methyl-1-(tri-*n*-butylstannyl)-2-pentene (139).[158]



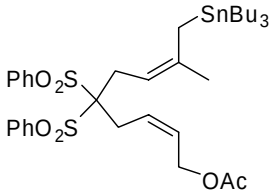
This compound was prepared from **138** following the general stannylation procedure. After purification by column chromatography (5:1 hexane-EtOAc), **139** was obtained as a vitreous solid (91%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.99-7.93 (m, 4H), 7.72-7.66 (m, 2H), 7.60-7.54 (m, 4H), 4.91 (t, *J* = 6.9 Hz, 1H), 4.35 (t, *J* = 6.9 Hz, 1H), 2.85 (t, *J* = 6.6 Hz, 2H), 1.57 (s, 2H), 1.49 (s, 3H), 1.43-1.30 (m, 6H), 1.27-1.13 (m, 6H), 0.89-0.63 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.33, 138.27, 134.41, 129.63, 129.00, 113.34, 84.74, 29.09 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.35 ($^{2}J(^{119}$Sn-C) = 54 Hz), 24.90, 22.41, 18.43, 13.70, 9.57 ($^{1}J(^{119}$Sn-C) = 316, $^{1}J(^{117}$Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{30}H_{46}O_4NaS_2{}^{116}Sn$ $[M+Na]^+$: 673.1753. Found: 673.1732.

(*Z*)-5,5-Bis(phenylsulfonyl)-2-methyl-1-(tri-*n*-butylstannyl)-2-pentene (141).[158]



This compound was prepared from **140** following the general stannylation procedure. After purification by column chromatography (5:1 hexane-EtOAc), **141** was obtained as a vitreous solid (91%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.00-7.92 (m, 4H), 7.72-7.65 (m, 2H), 7.60-7.53 (m, 4H), 4.72 (t, *J* = 7.1 Hz, 1H), 4.42 (t, *J* = 6.1 Hz, 1H), 2.79 (t, *J* = 6.6 Hz, 2H), 1.50 (s, 2H), 1.47 (s, 3H), 1.43-1.33 (m, 6H), 1.27-1.17 (m, 6H), 0.86-0.67 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.29, 138.24, 134.38, 129.60, 128.93, 112.70, 84.44, 29.02 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.34 ($^{2}J(^{119}$Sn-C) = 56 Hz), 25.87, 24.81, 15.57, 13.66, 9.81 ($^{1}J(^{119}$Sn-C) = 316, $^{1}J(^{117}$Sn-C) = 300 Hz). Anal. Calcd for $C_{30}H_{46}O_4S_2Sn$: C, 55.14; H, 7.09; S, 9.81. Found: C, 55.06; H, 6.92; S, 9.60. HRMS-ESI Calcd for $C_{30}H_{46}O_4NaS_2{}^{116}Sn$ $[M+Na]^+$: 673.1753. Found: 673.1760.

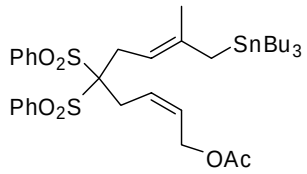
(2*Z*,7*Z*)-9-Acetoxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (132).



This compound was prepared from **141** and (*Z*)-1-acetoxy-4-bromo-2-butene[131] following the general procedure for alkylation. After purification by column chromatography (9:1 hexane-EtOAc), **132** was obtained as a vitreous solid (70%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.10-7.99 (m, 4H), 7.73-7.64 (m, 2H), 7.61-7.50 (m, 4H), 5.94-5.82 (m, 1H), 5.74-5.64 (m, 1H), 4.94 (t, *J* = 6.1 Hz, 1H), 4.56 (d, *J* = 6.6 Hz, 2H), 3.06 (d, *J* = 6.3 Hz, 2H), 2.85 (d, *J* = 6.3 Hz, 2H), 2.06 (s, 3H), 1.67 (s, 2H), 1.62 (s, 3H), 1.53-1.39 (m, 6H), 1.36-1.25 (m, 6H), 0.95-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.63, 141.15, 136.86, 134.40, 131.43, 128.41, 127.29, 125.77, 109.25, 90.65, 60.19, 29.04 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.83, 27.35 ($^{2}J(^{119}$Sn-C) = 55 Hz), 26.23, 20.87, 15.96, 13.64, 9.92 ($^{1}J(^{119}$Sn-C) = 315, $^{1}J(^{117}$Sn-C) = 301 Hz). HRMS-ESI Calcd for $C_{36}H_{54}O_6NaS_2{}^{116}Sn$ $[M+Na]^+$: 785.2277. Found: 785.2246.

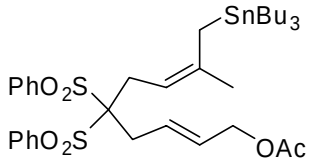
131 Reppe, W. *J. Liebigs Ann. Chem*. **1955**, 80-158.

(2*E*,7*Z*)-9-Acetoxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (133).



This compound was prepared from **139** and (*Z*)-1-acetoxy-4-bromo-2-butene[131] following the general procedure for alkylation. After purification by column chromatography (9:1 hexane-EtOAc), **133** was obtained as a vitreous solid (80%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.10-8.00 (m, 4H), 7.74-7.65 (m, 2H), 7.61-7.51 (m, 4H), 5.91-5.79 (m, 1H), 5.74-5.63 (m, 1H), 5.11 (t, *J* = 5.1 Hz, 1H), 4.54 (d, *J* = 6.6 Hz, 2H), 3.02 (d, *J* = 6.2 Hz, 2H), 2.95 (d, *J* = 6.6 Hz, 2H), 2.07 (s, 3H), 1.76 (s, 2H), 1.53 (s, 3H), 1.52-1.41 (m, 6H), 1.36-1.23 (m, 6H), 0.95-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.61, 141.48, 136.66, 134.45, 131.41, 128.43, 127.21, 125.62, 109.52, 90.71, 60.22, 29.09 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.62, 27.36 ($^{2}J(^{119}$Sn-C) = 54 Hz), 26.83, 22.82, 20.87, 18.97, 13.69, 9.59 ($^{1}J(^{119}$Sn-C) = 335, $^{1}J(^{117}$Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{36}H_{54}O_6NaS_2{}^{116}Sn$ $[M+Na]^+$: 785.2277. Found: 785.2300.

(2*Z*,7*E*)-9-Acetoxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (134).

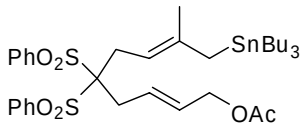


This compound was prepared from **141** and (*E*)-1-acetoxy-4-bromo-2-butene[130] following the general procedure for alkylation. After purification by column chromatography (9:1 hexane-EtOAc) was obtained as a vitreous solid (79%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.08-8.00 (m, 4H), 7.71-7.65 (m, 2H), 7.59-7.52 (m, 4H), 5.96-5.85 (m, 1H), 5.71-5.61 (m, 1H), 4.97 (d, *J* = 6.2 Hz, 1H), 4.51 (d, *J* = 6.2 Hz, 2H), 3.03 (d, *J* = 6.7 Hz, 2H), 2.82 (d, *J* = 6.4 Hz, 2H), 2.06 (s, 3H), 1.68-1.22 (m, 17H), 0.95-0.71 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.62, 141.00, 137.13, 134.37, 131.51, 129.33, 129.38, 127.09, 109.48, 90.77, 64.51, 32.03, 29.05 ($^{3}J(^{119}$Sn-C) = 20 Hz), 28.44, 27.36 ($^{2}J(^{119}$Sn-C) = 55 Hz), 26.27, 20.91, 15.91, 13.66, 9.93 ($^{1}J(^{119}$Sn-C) = 315,

130 Organ, M. G.; Cooper, L. R.; Soleymanzadeh, F.; Paul, T. *J. Org. Chem*. **2000**, *65*, 7959-7970.

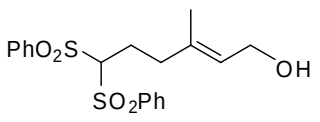
$^{1}J(^{117}\text{Sn-C})$ = 301 Hz). HRMS-ESI Calcd for $C_{36}H_{54}O_6NaS_2{}^{116}Sn$ $[M+Na]^+$: 785.2277. Found: 785.2303.

(2*E*,7*E*)-9-Acetoxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (135).

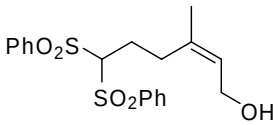


This compound was prepared from **139** and (*E*)-1-acetoxy-4-bromo-2-butene[130] following the general procedure for alkylation. After purification by column chromatography (9:1 hexane-EtOAc), **135** was obtained as a vitreous solid (80%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.08-8.00 (m, 4H), 7.73-7.65 (m, 2H), 7.60-7.52 (m, 4H), 5.87 (dt, *J* = 15.2, 6.7 Hz, 1H), 5.64 (dt, *J* = 15.5, 6.1 Hz, 1H), 5.13 (t, *J* = 6.6 Hz, 1H), 4.51 (d, *J* = 6.1 Hz, 2H), 3.00 (d, *J* = 6.7 Hz, 2H), 2.91 (d, *J* = 6.6 Hz, 2H), 2.07 (s, 3H), 1.76 (s, 2H), 1.54-1.40 (m, 9H), 1.35-1.23 (m, 6H), 0.96-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.59, 141.27, 136.96, 134.40, 131.49, 129.11, 128.38, 127.00, 109.81, 90.80, 64.43, 31.79, 29.09 ($^3J(^{119}\text{Sn-C})$ = 20 Hz), 28.37, 27.34 ($^2J(^{119}\text{Sn-C})$ = 53 Hz), 22.76, 20.89, 18.90, 13.69, 9.58 ($^1J(^{119}\text{Sn-C})$ = 315, $^1J(^{117}\text{Sn-C})$ = 300 Hz). HRMS-ESI Calcd for $C_{36}H_{54}O_6NaS_2{}^{117}Sn$ $[M+Na]^+$: 786.2289. Found: 786.2283.

(*E*)-6,6-Bis(phenylsulfonyl)-3-methyl-2-hexen-1-ol (143) and (*Z*)-6,6-bis(phenylsulfonyl)-3-methyl-2-hexen-1-ol (144).



143



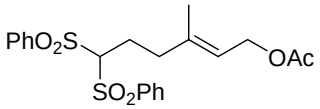
144

Compound **129** (3.67 g, 8.4 mmol) and $[PdCl_2(MeCN)_2]$ (81 mg, 0.33 mmol) were dissolved in THF (50 mL), the solution was stirred at 23ºC overnight and was filtered through Celite. After removal of the solvent the crude material was dissolved in MeOH (50 mL). To this solution, potassium carbonate (1.56g, 11.29 mmol) was added. The mixture was stirred at 23ºC for 3 h, after which a 0.2 M solution of HCl was added until pH = 7. The volume of methanol was reduced under vacuum and the organic phase was extracted with CH_2Cl_2. The isomers were separated by chromatography (1:1 hexane-EtOAc). The configuration was assigned by NOESY experiment.

143: White solid; mp: 101-103 ºC. Yield: 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.89 (m, 4H), 7.75-7.65 (m, 2H), 7.63-7.52 (m, 4H), 5.41 (bt, *J* = 6.6, 1H), 4.48 (m, 1H), 4.12 (d, *J* = 6.7 Hz, 2H), 2.36-2.23 (m, 4H), 1.53 (s, 3H), 1.40 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.86, 136.09, 134.50, 129.47, 129.07, 126.96, 81.65, 58.94, 37.06, 23.28, 15.49. Anal. Calcd for $C_{19}H_{22}O_5S_2$: C, 57.85; H, 5.62; S, 16.26. Found: C, 57.58; H, 5.53; S, 16.20. HRMS-ESI Cald for $C_{19}H_{22}O_5NaS_2$ $[M+Na]^+$: 417.0806. Found: 417.0799.

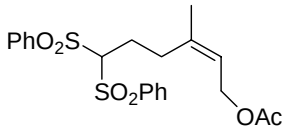
144: Yield: 13%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01–7.91 (m, 4H), 7.73-7.65 (m, 2H), 7.62-7.51 (m, 4H), 5.56 (bt, *J* = 6.7, 1H), 4.58 (t, *J* = 5.4 Hz, 1H), 4.12 (d, *J* = 7.5 Hz, 2H), 2.44 (t, *J* = 7.0 Hz, 2H), 2.34-2.27 (m, 2H), 1.66 (bs, 1H), 1.56 (s, 3H). ^{13}C NMR (100MHz,$CDCl_3$) δ 137.78, 136.86, 134.57, 129.64, 129.09, 127.38, 81.60, 58.37, 29.73, 23.35, 22.53. HRMS-ESI Cald for $C_{19}H_{22}O_5NaS_2$ $[M+Na]^+$: 417.0806. Found: 417.0807.

(*E*)-6,6-Bis(phenylsulfonyl)-3-methyl-2-hexenyl acetate (145).



This compound was obtained from **143** following the general acetylation procedure. The product was obtained as a white solid (90%) after purification by column chromatography (2:1 hexane-EtOAc); m.p. 84-86 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.90 (m, 4H), 7.75-7.65 (m, 2H), 7.63-7.53 (m, 4H), 5.36 (bt, *J* = 6.9 Hz, 1H), 4.55 (d, *J* = 6.9 Hz, 2H), 4.46 (t, *J* = 5.3 Hz, 1H), 2.40-2.26 (m, 4H), 2.06 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.91, 138.79, 137.98, 134.56, 129.59, 129.12, 122.12, 81.60, 60.98, 37.04, 23.22, 20.99, 15.71. Anal. Calcd for $C_{21}H_{24}O_6S_2$: C, 57.78; H, 5.54; S, 14.69. Found: C, 57.59; H, 5.50; S, 14.58. HRMS-ESI Cald for $C_{21}H_{24}O_6NaS_2$ $[M+Na]^+$: 459.0912. Found: 459.0900.

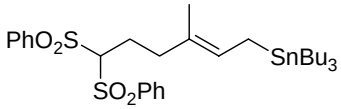
(*Z*)-6,6-Bis(phenylsulfonyl)-3-methyl-2-hexenyl acetate (147).



This compound was obtained from **144** following the general acetylation procedure. The crude material was purified by column chromatography (2:1 hexane-

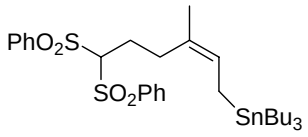
EtOAc) to afford the title compound as a colorless oil (97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.93 (m, 4H), 7.38-7.66 (m, 2H), 7.62-7.54 (m, 4H), 5.44 (bt, *J* = 7.4, 1H), 4.54 (d, *J* = 7.4 Hz, 2H), 4.47 (t, *J* = 5.4 Hz, 1H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.33-2.25 (m, 2H), 2.01 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.84, 139.47, 137.82, 134.60, 129.69, 129.11, 122.38, 82.03, 60.66, 30.14, 23.46, 22.63, 21.01. HRMS-ESI Cald for $C_{21}H_{24}O_6NaS_2$ $[M+Na]^+$: 459.0912. Found: 459.0902.

(*E*) -6,6-Bis(phenylsulfonyl)-3-methyl-1-(tributylstannanyl)-2-hexene (146).



This compound was obtained from **145** following the general stannylation procedure. Compound **146** was isolated as a vitreous solid (84%) after purification by column chromatography (2:1 hexane-EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01–7.93 (m, 4H), 7.72-7.65 (m, 2H), 7.61-7.52 (m, 4H), 5.40 (bt, *J* = 9.2, 1H), 4.43 (t, *J* = 4.9 Hz, 1H), 2.35-2.20 (m, 4H), 1.70 (d, *J* = 9.3 Hz), 1.57-1.39 (m, 6H), 1.35-1.25 (m, 6H), 0.94-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.13, 134.39, 129.66, 128.99, 127.22, 125.65, 82.30, 29.57, 29.15 (^{3}J(^{119}Sn-C) = 20 Hz), 27.34 (^{2}J(^{119}Sn-C) = 54Hz), 23.56, 22.22, 13.70, 10.95, 9.46 (^{1}J(^{119}Sn-C) = 313, (^{117}Sn-C) = 300Hz). HRMS-ESI Cald for $C_{31}H_{48}O_4Na^{120}SnS_2$ $[M+Na]^+$: 691.1914. Found: 691.1945.

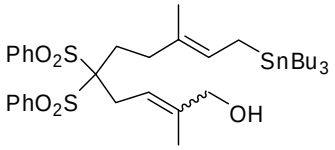
(*Z*)-6,6-Bis(phenylsulfonyl)-3-methyl-1-(tributylstannyl)-2-hexene (148).



This compound was prepared from **147** following the general stannylation procedure. The product was obtained as a vitreous solid (70%) after purification by column chromatography (2:1 hexane-EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02-7.92 (m, 4H), 7.23-7.66 (m, 2H), 7.63-7.53 (m, 4H), 5.33 (bt, *J* = 8.8 Hz, 1H), 4.49 (m, 1H), 2.24 (m, 4H), 1.64 (d, *J* = 9.1 Hz, 2H), 1.57-1.45 (m, 6H), 1.40 (s, 3H), 1.36-1.25 (m, 6H), 0.96-0.72 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.19, 134.38, 129.62, 128.99, 127.11, 125.78, 82.09, 37.54, 29.15 (^{3}J(^{119}Sn-C) = 20 Hz), 27.32 (^{2}J(^{119}Sn-C) =

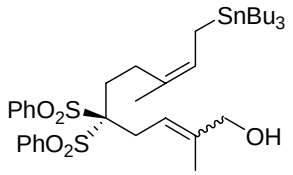
54Hz), 24.03, 14.81, 13.69, 10.96, 9.49. HRMS-ESI Cald for $C_{31}H_{48}O_4Na^{120}SnS_2$ $[M+Na]^+$: 691.1914. Found: 691.1932.

(2*E*)-6,6-Bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadien-10-ol (149).



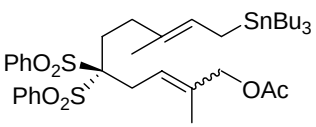
This compound was obtained from **146** and 2-methyl-2-vinyloxirane following the general procedure for nucleophilic opening of vinyl epoxides as a (53:47) mixture of alcohols that resulted inseparable. The mixture was purified by column chromatography (2:1 hexane-EtOAc) to give the title compound (72%) as a vitreous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.02 (m, 4H, major and minor), 7.56-7.68 (m, 2H, major and minor), 7.64-7.54 (m, 4H, major and minor), 5.69 (t, *J* = 5.8 Hz, 1H, major), 5.42 (t, *J* = 6.7 Hz, 1H, minor), 5.35 (t, *J* = 9.3 Hz, 1H, major and minor), 4.13 (d, *J* = 5.8 Hz, 2H, major), 4.05 (d, *J* = 6.1 Hz, 2H, minor), 3.12 (d, *J* = 6.1 Hz, 2H, major), 3.04 (d, *J* = 6.1 Hz, 2H, minor), 2.30 (m, 4H, major and minor), 1.86 (s, 2H, major and minor), 1.74 (t, *J* = 6.7 Hz, 1H, major and minor), 1.69-1.24 (m, 18H, major and minor), 0.96-0.75 (m, 15H, major and minor). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) 139.23 (C, major), 139.16 (C, minor), 137.17 (C, minor), 136.89 (C, major), 134.48 (CH, minor), 134.45 (CH, major), 131.38 (CH, minor), 131.35 (CH, major), 128.52 (CH, minor), 128.48 (CH, major), 128.51 (CH, minor), 128.48 (CH, major), 127.09 (C, major), 127.02 (C, minor), 124.92 (CH, minor), 124.89 (CH, major), 118.43 (CH, minor), 116.70 (CH, major), 91.86 (C, minor), 91.50 (C, major), 68.39 (CH_2, major), 61.45 (CH_2, minor), 33.53 (CH_2, minor), 33.25 (CH_2, major), 29.22 (CH_2, major and minor), 28.61 (CH_2, minor), 27.71 (CH_2, major), 27.36 (CH_2, major and minor), 27.15 (CH_2, major), 26.72 (CH_2, minor), 21.84 (CH_3, major and minor), 15.55 (CH_3, major and minor), 14.16 (CH_3, minor), 13.73 (CH_3, major), 10.80 (CH_2, major and minor), 9.43 (CH_2, major and minor).HRMS-ESI Cald for $C_{36}H_{56}O_5NaS_2{}^{116}Sn$ $[M+Na]^+$: 771.2484. Found: 771.2505.

(2*Z*)-6,6-Bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadien-10-ol (150).



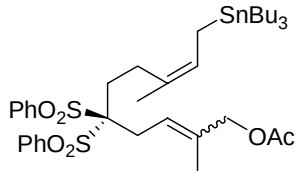
This compound was obtained from **148** and 2-methyl-2-vinyloxirane following the general procedure for nucleophilic opening of vinyl epoxides as a (68:32) mixture of alcohols that resulted inseparable. The mixture was purified by column chromatography (2:1 hexane-EtOAc) to yield the title compound as a vitreous solid (72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.03 (m, 4H, major and minor), 7.76-7.67 (m, 2H, major and minor), 7.63-7.55 (m, 4H, major and minor), 5.72 (t, *J* = 5.5 Hz, 1H, major), 5.45 (t, *J* = 6.4 Hz, 1H, minor), 5.35 (t, *J* = 9.1 Hz, 1H, major and minor), 4.13 (d, *J* = 5.8 Hz, 2H, minor), 4.03 (d, *J* = 6.1 Hz, 2H, major), 3.15 (d, *J* = 7.3 Hz, 2H, minor), 3.07 (d, *J* = 5.8 Hz, 2H, major), 2.42-2.22 (m, 4H, major and minor), 1.75 (t, *J* = 5.5 Hz, 1H, major and minor), 1.70-1.22 (m, 20 H, major and minor), 0.98-0.73 (m, 15H, major and minor). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) 139.10 (C, major and minor), 137.22 (C, minor), 136.98 (C, major), 134.50 (CH, minor), 134.46 (CH, major), 131.42 (CH, minor), 131.39 (CH, major), 128.52 (CH, minor), 128.49 (CH, major), 126.82 (C, major), 126.79 (C, minor), 125.76 (CH, minor), 125.69 (CH, major), 118.53 (CH, major and minor), 116.70 (CH, major and minor), 91.81 (C, minor), 91.43 (C, major), 68.30 (CH_2, major), 61.46 (CH_2, minor), 29.20 (CH_2, major and minor), 27.41 (CH_2, major and minor), 27.33 (CH_2, minor), 27.29 (CH_2, major), 26.92 (CH_2, major), 26.55 (CH_2, minor), 25.58 (CH_2, minor), 25.29 (CH_2, major), 22.86 (CH_3, minor), 22.81 (CH_3, major), 21.82 (CH_3, major and minor), 14.11 (CH_3, minor), 13.78 (CH_3, major), 10.76 (CH_2, major), 10.74 (CH_2, minor), 9.39 (CH_2, major and minor). HRMS-ESI Cald for $C_{36}H_{56}O_5NaS_2{}^{116}Sn$ $[M+Na]^+$: 771.2484. Found: 771.2520.

(2*E*)-10-Acetoxy-6,6bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadiene (151).



This compound was obtained from **149** following the general acetylation procedure. The product was isolated as a colorless oil (87%) after purification by column chromatography (4:1 hexane-EtOAc). Mixture of isomers 63:37. ^{1}H NMR (400 MHz, $CDCl_3$)8.10-8.00(m, 4H, major and minor), 7.75-7.65 (m, 2H, major and minor), 7.61-7.52 (m, 4H, major and minor), 5.72 (bt, *J* = 5.5 Hz, 1H, major), 5.61 (bt, *J* = 5.8 Hz, 1H, minor), 5.35 (overlapping t, *J* = 9.3 Hz, 1H, major), 5.30 (overlapping t, *J* = 9.6 Hz, 1H, minor), 4.51 (s, 2H, minor), 4.48 (s, 2H, major), 3.07 (d, *J* = 6.1 Hz, 2H, minor), 2.99 (d, *J* = 6.1 Hz, 2H, major), 2.26 (m, 4H, major and minor), 2.09 (s, 3H, major), 2.06 (s, 3H, minor), 1.79 (s, 2H, major and minor), 1.67-1.22 (18H, major and minor), 0.94-0.72 (15H, major and minor). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 170.71 (C, minor), 170.68 (C, major), 137.00 (C, minor), 136.83 (C, major), 134.45 (CH, major and minor), 134.37 (C, major and minor), 131.39 (CH, major and minor), 128.47 (CH, major and minor), 127.13 (C, minor), 127.02 (C, minor), 125.02 (CH, major), 124.86 (CH, minor), 120.96 (CH, minor), 119.63 (CH, major), 91.31 (C, major), 91.15 (C, minor), 69.23 (CH_2, major), 62.82 (CH_2, minor), 33.28 (CH_2, major and minor), 29.20 (CH_2, major and minor), 28.00 (CH_2, minor), 27.58 (CH_2, major), 27.33 (CH_2, major and minor), 26.98 (CH_2, minor), 26.71 (CH_2, major), 21.80 (CH_3, major and minor), 20.87 (CH_3, major), 20.76 (CH_3, minor), 15.51 (CH_3, minor), 15.45 (CH_3, major), 14.34 (CH_3, minor), 13.73 (CH_3, major), 10.84 (CH_2, major), 10.80 (CH_2, minor), 9.46 (CH_2, major), 9.42 (CH_2, minor). HRMS-ESI Cald for $C_{38}H_{58}O_6NaS_2{}^{116}Sn$ $[M+Na]^+$: 813.2590. Found: 813.2614.

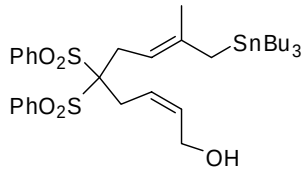
(2*Z*)-10-Acetoxy-6,6bis(phenylsulfonyl)-3,9-dimethyl-1-(tri-*n*-butylstannyl)-2,8-decadiene (152).



This compound was prepared from **150** following the general acetylation procedure. The product was obtained as a colourless oil (90%) after purification by column chromatography (4:1 hexane-EtOAc). Mixture of isomers 68:32. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12-7.99 (m, 4H, major and minor), 7.75-7.65 (m, 2H, major and minor), 7.61-7.51 (m, 4H, major and minor), 5.73 (bt, J = 6.1 Hz, 1H, major), 5.62 (bt, *J* = 6.1 Hz, 1H, minor), 5.33 (t, *J* = 8.5 Hz , 1H, major and minor), 4.51 (s, 2H, minor),

4.46 (s, 2H, major), 3.11 (d, J = 6.7 Hz, 2H, minor), 3.03 (d, J = 6.4 Hz, 2H, major), 2.37-2.21(m, 4H, major and minor), 2.08 (s, 3H, major), 2.06 (s, 3H, minor), 1.69-1.23 (m, 20H, major and minor), 0.93-0.74 (m, 15H, major and minor). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 170.60 (C, major and minor), 137.05 (C, minor), 136.92 (C, major), 134.49 (CH, major and minor), 134.32 (C, major and minor), 131.44 (CH, major and minor), 128.47 (CH, major and minor), 126.92 (C, minor), 126.77 (C, minor), 125.73 (CH, major), 125.70 (CH, minor), 121.05 (CH, minor), 119.48 (CH, major), 91.24 (C, major), 91.08 (C, minor), 68.92 (CH_2, major), 62.84 (CH_2, minor), 29.19 (CH_2, major and minor), 27.38 (CH_2, major and minor), 27.16 (CH_2, minor), 26.95 (CH_2, major), 26.72 (CH_2, minor), 26.44 (CH_2, major), 25.44 (CH_2, minor), 25.33 (CH_2, major), 22.85 (CH_3, minor), 22.75 (CH_3, major), 21.78 (CH_3, major and minor), 20.84 (CH_3, major), 20.76 (CH_3, minor), 10.79 (CH_2, major), 10.75 (CH_2, minor), 9.40 (CH_2, major), 9.38 (CH_2, minor). HRMS-ESI Cald for $C_{38}H_{58}O_6NaS_2{}^{116}Sn$ $[M+Na]^+$: 813.2590. Found: 813.2602.

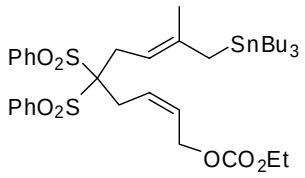
(2*E*,7*Z*)-9-Hydroxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (172).



To a suspension of potassium carbonate (360 mg, 1.20 mmol) in MeOH (20 mL) at 0ºC was added **133** (1.66 g, 2.17 mmol). The reaction was stirred from 0ºC to 23ºC for 1 h after which a 0.2 M solution of HCl was added until pH = 7. The volume of MeOH was reduced under vacuum and after addition of CH_2Cl_2 the organic phase was submitted to usual extractive work-up (CH_2Cl_2/H_2O). The crude mixture was purified by column chromatography (3:1 hexane-EtOAc) to yield **172** as a colorless oil (1.12 g, 71%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.10-8.02 (m, 4H), 7.76-7.68 (m, 2H), 7.65-7.53 (m, 4H), 5.87-5.77 (m, 1H), 5.76-5.67 (m, 1H), 5.13 (t, J = 6.4 Hz, 1H), 4.17 (t, J = 6.1 Hz, 2H), 3.05 (d, J = 6.7 Hz, 2H), 2.98 (d, J = 6.7 Hz, 2H), 1.77 (s, 2H), 1.73-1.67 (m, 1H), 1.56 (s, 3H), 1.54-1.44 (m, 6H), 1.38-1.25 (m, 6H), 0.97-0.79 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.51, 136.86, 134.49, 132.39, 131.43, 128.49, 123.47, 109.78, 91.28, 58.48, 29.12 (^3J(^{119}Sn-C) = 20 Hz), 28.14, 27.39 (^2J(^{119}Sn-C) = 55 Hz), 26.90,

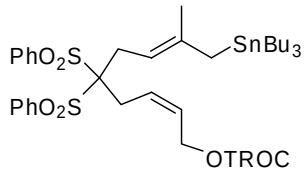
22.83, 18.98, 13.73, 9.63 ($^{1}J(^{119}$Sn-C) = 314, $^{1}J(^{117}$Sn-C) = 301 Hz). HRMS-ESI Calcd for $C_{34}H_{52}O_5NaS_2{}^{120}Sn$ $[M+Na]^+$: 747.2176. Found: 747.2206.

(2*E*,7*Z*)-9-Ethoxycarbonyloxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (174).



To a solution of **172** (180 mg, 0.25 mmol) and DMAP (2 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) at 0ºC was added *i*-$PrEt_2N$ (0.09 mL, 0.51 mmol) and ethyl chloroformate (0.05 mL, 0.51 mmol). The resulting mixture was stirred at 23ºC for 3 h. After extractive workup (CH_2Cl_2/H_2O) and column chromatography (4:1 hexane-EtOAc), **174** was obtained as a colorless oil (189 mg, 93%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.12-8.03 (m, 4H), 7.76-7.65 (m, 2H), 7.63-7.54 (m, 4H), 5.95-5.85 (m, 1H), 5.80-5.71 (m, 1H), 5.14 (br t, *J* = 6.7 Hz, 1H), 4.61 (d, *J* = 6.7 Hz, 2H), 4.23 (q, *J* = 7.3 Hz, 2H), 3.04 (d, *J* = 6.1 Hz, 2H), 2.98 (d, *J* = 7.0 Hz, 2H), 1.79 (s, 2H), 1.59-1.09 (m, 18H), 0.99-0.77 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.99, 141.63, 136.62, 134.48, 131.45, 128.44, 126.71, 126.16, 109.45, 90.68, 64.11, 63.24, 29.11 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.55, 27.38 ($^{2}J(^{119}$Sn-C) = 54 Hz), 26.80, 22.84, 19.00, 14.31, 13.72, 9.60 ($^{1}J(^{119}$Sn-C) = 314, $^{1}J(^{117}$Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{37}H_{56}O_7NaS_2{}^{120}Sn$ $[M+Na]^+$: 819.2387. Found: 819.2353.

(2*E*,7*Z*)-9-2,2,2-Trichloroethoxycarbonyloxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (175).

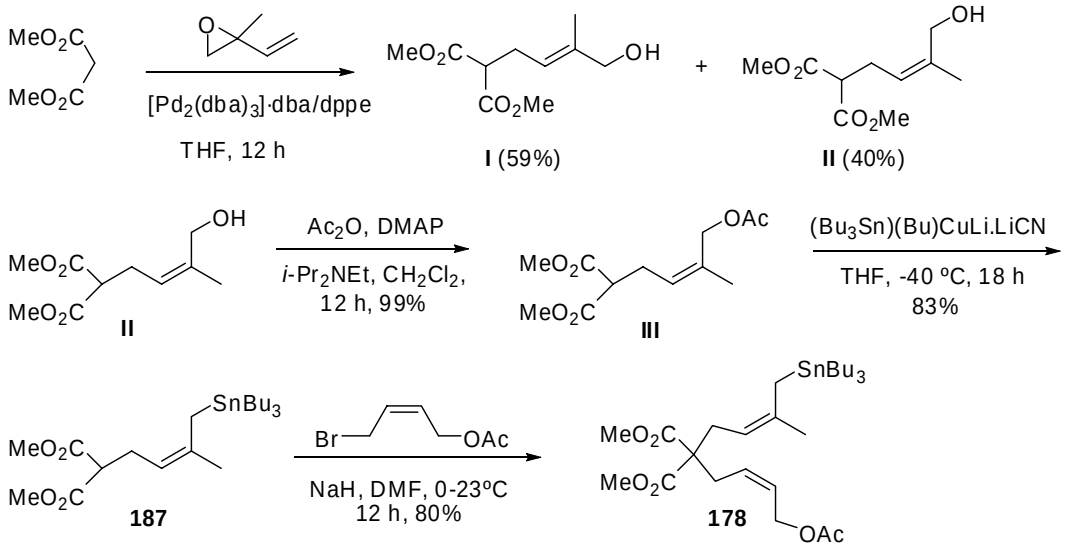


To a solution of **172** (250 mg, 0.34 mmol) and DMAP (2 gm, 0.20 mmol) in CH_2Cl_2 (6 mL) at 0ºC was added *i*-$PrEt_2N$ (0.12 mL, 0.69 mmol) and 2,2,2-trichloroethyl chloroformate (0.09 mL, 0.69 mmol). The resulting mixture was stirred at 23ºC for 3 h. After extractive workup (CH_2Cl_2/H_2O) and chromatography (4:1, hexane-EtOAc), **175** was obtained as a colorless oil (286 mg, 92%).^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.14-8.02 (m, 4H), 7.77-7.68 (m, 2H), 7.66-7.55 (m, 4H), 6.03-5.91 (m, 1H),

5.84-5.74 (m, 1H), 5.15 (br t, J = 6.7 Hz, 1H), 4.81 (s, 2H), 4.72 (d, J = 6.7 Hz, 2H), 3.06 (d, J = 6.2 Hz, 2H), 2.99 (d, J = 6.4 Hz, 2H), 1.79 (s, 2H), 1.56 (s, 3H), 1.55-1.43 (m, 6H), 1.38-1.26 (m, 6H), 0.98-0.78 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.83, 141.80, 136.56, 134.56, 131.52, 131.44, 128.53, 127.24, 125.79, 109.37, 94.40, 90.60, 76.87, 64.39, 29.12 (^3J(^{119}Sn-C) = 20 Hz), 27.61, 27.40 (^2J(^{119}Sn-C) = 54 Hz), 26.83, 22.86, 19.01, 13.74, 9.62 (^1J(^{119}Sn-C) = 315, ^1J(^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{37}H_{53}O_7NaS_2Cl_3{}^{120}Sn$ $[M+Na]^+$: 921.1218. Found: 921.1204.

Dimethyl 2-((*Z*)-4-Acetoxy-2-butenyl)-2-((*Z*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (178).

The title compound was obtained according to the following scheme:



Compounds **I** and **II** were prepared from dimethyl malonate and 2-methyl-2-vinyloxirane following the general procedure for nucleophilic opening of vinyl epoxides. They were obtained as mixture of regioisomers and were separated by column chromatography (3:1 to 2:1 hexane-EtOAc).

Dimethyl (*E*)-2-(4-Hydroxy-3-methyl-2-butenyl)malonate (I).[159]

Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.28 (tt, J = 7.6, 1.2 Hz, 1H), 3.90 (s, 2H), 3.66 (s, 6H), 3.34 (t, J = 7.6 Hz, 1H), 2.60 (t, J = 7.4 Hz, 2H), 2.10 (br s, 1H), 1.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.46, 138.28, 120.24, 68.11, 52.49, 51.53, 27.04, 13.57. HRMS-ESI Cald for $C_{10}H_{16}O_5Na$ $[M+Na]^+$: 239.0895. Found: 239.0900.

159 Described as mixture of *E*/*Z* isomers in: Ross, J.; Xiao, J. *Chem. Eur. J.* **2003**, *9*, 4900-4906.

Dimethyl (*Z*)-2-(4-Hydroxy-3-methyl-2-butenyl)malonate (II).[160]

Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.09 (t, *J* = 7.7 Hz, 1H), 4.00 (s, 2H), 3.63 (s, 6H), 3.33 (t, *J* = 7.4 Hz, 1H), 2.57 (t, *J* = 7.6 Hz, 2H), 1.89 (br s, 1H), 1.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.59, 138.61, 122.74, 61.30, 52.62, 51.70, 27.18, 21.74. HRMS-ESI Cald for $C_{10}H_{16}O_5Na$ $[M+Na]^+$: 239.0895. Found: 239.0887.

Dimethyl (*Z*)-2-(4-Acetoxy-3-methyl-2-butenyl)malonate (III).

This compound was prepared following the general stannylation procedure. The product was obtained as a colerless solid (99%) after purification by column chromatography (3:1 hexane-EtOAc). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.26 (t, *J* = 7.6 Hz, 1H), 4.52 (s, 2H), 3.66 (s, 6H), 3.33 (td, *J* = 7.5, 1.2 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.98 (s, 3H), 1.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.78, 169.11, 133.35, 125.27, 62.70, 52.44, 51.58, 27.11, 20.76. HRMS-ESI Cald for $C_{12}H_{18}O_6Na$ $[M+Na]^+$: 281.1001. Found: 281.0993.

Dimetyl 2-[(*Z*)-3-Methyl-4-tributylstannyl-2-butenyl]malonate (187).[161]

This compound was prepared following the general stannylation procedure. The product was obtained as a colorless oil (83%) after purification by column chromatography (10:1 hexane-EtOAc). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.74 (t, *J* = 7.1 Hz, 1H), 3.71 (s, 6H), 3.35 (t, *J* = 7.7 Hz, 1H), 2.52 (t, *J* = 7.2 Hz, 2H), 1.73 (s, 2H), 1.65 (s, 3H), 1.58-1.44 (m, 6H), 1.38-1.25 (m, 6H), 0.99-0.77 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.68, 138.92, 114.42, 52.33, 52.03, 29.08 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.86, 27.36 ($^{2}J(^{119}$Sn-C) = 55 Hz), 25.97, 15.42, 13.62, 9.70 ($^{1}J(^{119}$Sn-C) = 313, (^{117}Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{22}H_{42}O_4Na^{120}Sn$ $[M+Na]^+$: 513.2003. Found: 513.2007.

Dimethyl [2-((*Z*)-4-Acetoxy-2-butenyl)-2-((Z)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)]malonate (178).

The title compound was obtained from **187** and (*Z*)-1-acetoxy-4-bromo-2-butene following the general procedure for alkylation. After purification by column chromatography (9:1 hexane-EtOAc), **178** was obtained as a colorless oil (80%). ^{1}HNMR (400 MHz, $CDCl_3$) δ 5.69-5.58 (m, 1H), 5.55-5.44 (m, 1H), 4.55 (overlapping

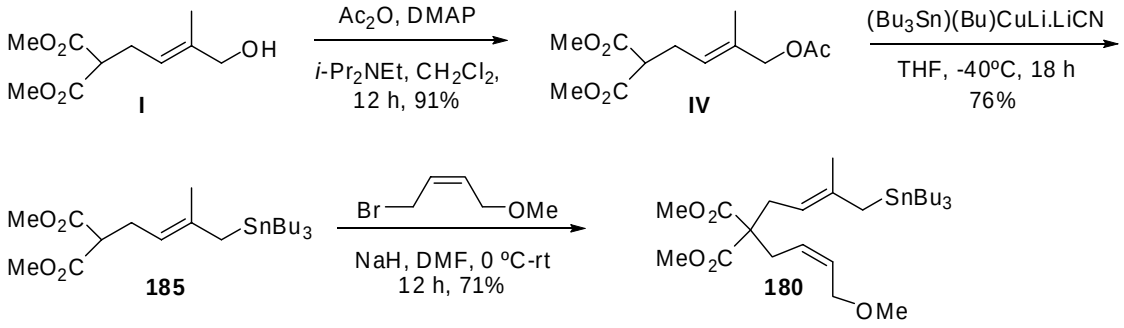
160 Bohmer, J.; Fortsch, W.; Shobert, R. Synlett **1997**, *9*, 1073-1074.

161 Described as a *E/Z* mixture in: Miura, K.; Fujisawa, N.; Hosomi, A. *J. Org. Chem*. **2004**, *69*, 2424-2430.

triplet, J = 7.0 Hz, 1H), 4.52 (d, J = 6.4 Hz, 2H), 3.69 (s, 6H), 2.68 (d, J = 7.6 Hz, 2H), 2.53 (d, J = 7.0 Hz, 2H), 2.04 (s, 3H), 1.62 (s, 2H), 1.58 (s, 3H), 1.47-1.34 (m, 6H), 1.30-1.17 (m, 6H), 0.95-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.47, 170.79, 139.96, 128.38, 127.13, 127.13, 111.94, 60.23, 57.66, 52.38, 31.47, 30.54, 29.08 (^3J(^{119}Sn-C) = 20 Hz), 27.36 (^2J(^{119}Sn-C) = 54 Hz), 26.23, 20.89, 15.61, 13.65, 9.77 (^1J(^{119}Sn-C) = 314, (^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{28}H_{50}O_6Na^{116}Sn$ $[M+Na]^+$: 621.2523. Found: 621.2493.

Dimethyl 2-((*Z*)-4-Methoxy-2-butenyl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (180).

The title compound was obtained according to the following scheme:



Dimethyl (*E*)-2-(4-Acetoxy-3-methyl-2-butenyl)malonate (IV).[162]

Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.32 (td, J = 7.3, 1.0 Hz, 1H), 4.36 (s, 2H), 3.66 (s, 6H), 3.34 (t, J = 7.6 Hz, 1H), 2.58 (t, J = 7.5 Hz, 2H), 1.99 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.64, 169.23, 133.45, 123.88, 69.38, 52.44, 51.23, 27.11, 20.83, 13.88. HRMS-ESI Cald for $C_{12}H_{18}O_6Na$ $[M+Na]^+$: 281.1001. Found: 281.1000.

Dimetyl 2-[(*E*)-3-Methyl-4-tributylstannyl-2-butenyl]malonate (185).[161]

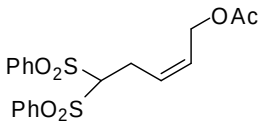
Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.88 (t, J = 7.5 Hz, 1H), 3.72 (s, 6H), 3.33 (t, J = 7.6 Hz, 1H), 2.58 (t, J = 7.5 Hz, 2H), 1.73 (s, 2H), 1.63 (s, 3H), 1.57-1.41 (m, 6H), 1.37-1.24 (m, 6H), 0.95-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.68, 139.01, 114.82, 52.37, 29.11 (^3J(^{119}Sn-C) = 20 Hz), 27.94, 27.34 (^2J(^{119}Sn-C) = 53 Hz), 22.25, 18.52, 13.68, 9.40 (^1J(^{119}Sn-C) = 314, (^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{22}H_{42}O_4Na^{116}Sn$ $[M+Na]^+$: 509.1998. Found: 509.1981.

162 Noboru, O.; Hamamoto, I.; Kaji, A. *J. Chem. Soc., Perkin Trans. 1*, **1986**, 1439-1443.

Dimethyl 2-((*Z*)-4-Acetoxy-2-butenyl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (180).

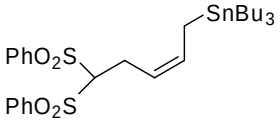
The title compound was obtain from **185** and (*Z*)-1-metoxy-4-bromo-2-butene[163] following the general procedure for alkylation. After purification by column chromatography (8:1 hexane-EtOAc) was obtained as a colorless oil (80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70-5.61 (m, 1H), 5.50-5.40 (m, 1H), 4.76 (t, *J* = 7.6 Hz, 1H), 3.97 (d, *J* = 6.2 Hz, 2H), 3.71 (s, 6H), 3.33 (s, 3H), 2.65 (d, *J* = 7.9 Hz, 2H), 2.63 (d, *J* = 7.6 Hz, 2H), 1.74 (s, 2H), 1.59 (s, 3H), 1.54-1.40 (m, 6H), 1.36-1.24 (m, 6H), 0.97-0.73 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 171.60, 139.94, 129.98, 126.42, 112.47, 68.06, 57.98, 57.80, 52.33, 31.40, 30.44, 29.11 (^{3}J(^{119}Sn-C) = 20 Hz), 27.36 (^{2}J(^{119}Sn-C) = 55 Hz), 22.54, 18.71, 13.69, 9.44 (^{1}J(^{119}Sn-C) = 313, (^{117}Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{27}H_{50}O_5Na^{120}Sn$ $[M+Na]^+$: 597.2578. Found: 597.2593.

(*Z*)-5,5-Bis(phenylsulfonyl)-2-penten acetate (182).[164]



White solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.00-7.95 (m, 4H), 7.77-7.69 (m, 2H), 7.65-7.56 (m, 4H), 5.73 (dtt, *J* = 10.8, 7.0, 1.5 Hz, 1H), 5.62 (dtt, *J* = 10.8, 6.7, 1.5 Hz, 1H), 4.68 (t, *J* = 6.1 Hz, 1H), 4.51 (d, *J* = 6.7 Hz, 2H), 3.03 (d, *J* = 6.7 Hz, 2H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.67, 137.75, 134.69, 129.64, 129.16, 127.92, 127.46, 83.28, 59.77, 23.88, 20.91.

(*Z*)-5,5-Bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-pentene (183).[165]



This compound was prepared from **182** following the general stannylation procedure. The product was obtained as a vitreous solid (78%) after purification by

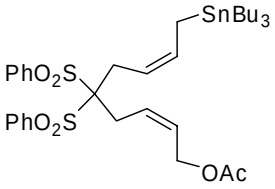
163 Organ, M. G.; Cooper, J. T.; Rogers, L. R.; Soleymanzadeh, F.; Paul, T. *J. Org. Chem*. **2000**, *65*, 7959-7970.

164 Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222.

165 Fernández-Rivas, C.; Méndez, M.; Nieto-Overhuber, C.; Echavarren, A. M. *J. Org. Chem*. **2002**, *67*, 5197-5201.

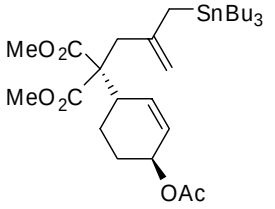
column chromatography (4:1 hexane-EtOAc). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.05-7.97 (m, 4H), 7.76-7.67 (m, 2H), 7.64-7.53 (m, 4H), 5.67 (q, *J* = 9.4 Hz, 1H), 5.11-5.02 (m, 1H), 4.46 (t, *J* = 5.7 Hz, 1H), 2.87 (t, *J* = 6.4 Hz, 2H), 1.70-1.24 (m, 8H), 0.99-0.75 (m, 15H).

(2*Z*,7*Z*)-9-Acetoxy-5,5-bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2,7-nonadiene (184).



The title compound was obtained from **183** and (*Z*)-1-acetoxy-4-bromo-2-butene following the general procedure for alkylation. After purification by column chromatography (8:1 hexane-EtOAc), **184** was obtained as a vitreous solid (78%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.14-8.05 (m, 4H), 7.76-7.67 (m, 2H), 7.63-7.54 (m, 4H), 5.96-5.87 (m, 1H), 5.85-5.67 (m, 2H), 5.35-5.23 (m, 1H), 4.58 (d, *J* = 6.7 Hz, 2H), 3.08 (d, *J* = 6.4 Hz, 2H), 2.93 (d, *J* = 6.7 Hz, 2H), 2.09 (s, 3H), 1.64 (d, *J* = 9.3 Hz, 2H), 1.54-1.39 (m, 6H), 1.36-1.23 (m, 6H), 0.97-0.73 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69, 136.58, 134.52, 134.02, 131.46, 128.51, 127.37, 125.63, 113.45, 90.46, 60.25, 29.11 ($^3J(^{119}$Sn-C) = 20 Hz), 27.34 ($^2J(^{119}$Sn-C) = 53 Hz), 26.82, 26.31, 20.90, 13.70, 11.23, 9.61 ($^1J(^{119}$Sn-C) = 319, $^1J(^{117}$Sn-C) = 305 Hz). HRMS-ESI Calcd for $C_{35}H_{52}O_6NaS_2{}^{120}Sn$ $[M+Na]^+$: 775.2125. Found: 775.2122.

Dimethyl 2-(*trans*-4-Acetoxycyclohex-2-en-1-yl)-2-(2-methyltri-*n*-butylstannyl-2-propenyl)malonate (191).



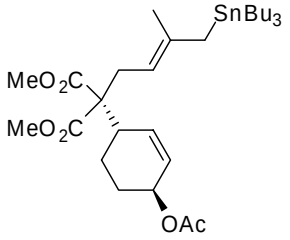
To a suspension of NaH (60% mineral oil, 18 mg, 0.44 mmol) in DMF (10 mL) was added dimethyl-1-(2-propenyl-2-tri-*n*-butylstannyl)malonate[166] (210 mg, 0.44 mmol) at 0ºC. After 10 minutes *cis*-1-acetoxy-4-chloro-2-cyclohexene[167] (80 mg, 0.45

166 Martín-Matute, B.; Buñuel, E.; Méndez, M.; Nieto-Oberhuber, C.; Cárdenas, D.; Echavarren, A. M. *J. Organomet. Chem*. **2003**, *687*, 410-419.

167 Bäckvall, J.-E.; Nyström, J.-E.; Nordberg, R. E. *J. Am. Chem. Soc*. **1985**, *105*, 3676- 3686.

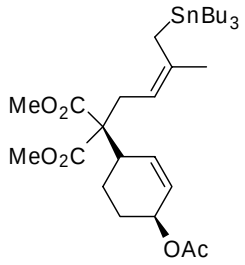
mmol) was added and the resulting solution was stirred overnight at 70 ºC. The reaction was quenched by addition of water at 0ºC. After extractive work-up (Et_2O/H_2O) the crude material was purified by column chromatography (15:1 hexane-EtOAc) to yield **191** as a colorless oil (198 mg, 73%). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.97 (dq, *J* = 10.5, 1.7 Hz, 1H), 5.64 (dq, *J* = 10.5, 2.0 Hz, 1H), 5.26 (m, 1H), 4.66 (d, *J* = 1.4, $^4J(^{119}$Sn-H) = 19.4 Hz, 1H), 4.46 (d, *J* = 1.2, $^4J(^{119}$Sn-H) = 19.5 Hz, 1H), 3.71 (s, 3H), 3.68 (s, 3H), 3.07 (m, 1H), 4.09 (d, *J* = 4.1 Hz, 2H), 2.18-2.10 (m, 1H), 2.05 (s, 3H), 1.99-1.90 (m, 1H), 1.74 (d, *J* = 2.6 Hz, 2H), 1.63-1.44 (m, 8H), 1.40-1.29 (m, 6H), 1.02-0.83 (m, 15H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 170. 85, 170.49, 170.44, 145.35, 132.04, 128.04, 108.71, 69.66, 61.17, 51.91, 51.77, 40.11, 39.67, 29.06 ($^3J(^{119}$Sn-C) = 20 Hz), 28.46, 27.38 ($^2J(^{119}$Sn-C) = 56 Hz), 22.87, 21.03, 20.24, 13.44, 9.39 ($^1J(^{119}$Sn-C) = 317, (^{117}Sn-C) = 303 Hz). Anal. Calcd for $C_{29}H_{50}O_6Sn$: C, 56.78; H, 8.22. Found: C, 56.76; H, 7.96. HRMS-ESI Calcd for $C_{29}H_{50}O_6Na^{120}Sn$ $[M+Na]^+$: 637.2527. Found: 637.2532.

Dimethyl 2-(*trans*-4-Acetoxycyclohex-2-en-1-yl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (186).



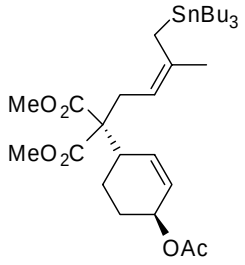
This compound was obtained by alkylation of 2-[(*E*)-3-methyl-4-tributylstannyl-2-butenyl]malonate with *cis*-1-acetoxy-4-chloro-2-cyclohexene following the procedure described for compound **191**. The product was obtained as colorless oil (73%) after column chromatography (15:1 hexane-EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (dd, *J* = 10.5, 1.7 Hz, 1H), 5.62 (dq, *J* = 10.5, 2.0 Hz, 1H), 5.28 (m, 1H); 4.80 (d, *J* = 7.8 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.05 (m, 1H), 2.75-2.58 (m, 2H), 2.19-2.09 (m, 1H), 2.06 (s, 3H), 1.92-1.83 (m, 1H), 1.75 (s, 2H), 1.63-1.53 (m, 2H), 1.59 (s, 3H), 153-1.41 (m, 6H), 1.37-1.25 (m, 6H), 0.96-0.74 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.21, 170.84, 170.83, 139.52, 132.18, 127.87, 112.65, 69.84, 61.19, 52.16, 52.00, 38.31, 31.40, 29.13 ($^3J(^{119}$Sn-C) = 20 Hz), 28.48, 27.37 ($^2J(^{119}$Sn-C) = 55 Hz), 22.52, 21.32, 18.72, 13.71, 9.45 ($^1J(^{119}$Sn-C) = 313, (^{117}Sn-C) = 299 Hz). Anal. Calcd for $C_{30}H_{52}O_6Sn$: C, 57.43; H, 8.35. Found: C, 57.25; H, 8.10. HRMS-ESI Calcd for $C_{30}H_{52}O_6Na^{120}Sn$ $[M+Na]^+$: 651.2684. Found: 651.2667.

Dimethyl 2-(*cis*-4-Acetoxycyclohex-2-en-1-yl)-2-((*Z*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (188).



To a suspension of NaH (60% mineral oil, 24 mg, 0.61 mmol) in DMF (8 mL) was added 2-[(*Z*)-3-methyl-4-tributylstannyl-2-butenyl]malonate (300 mg, 0.61 mmol) at 0ºC. After 10 minutes a mixture of $[Pd_2(dba)_3]\cdot dba$ (18 mg, 0.015 mmol), PPh_3 (8 mg, 0.031 mmol) and *cis*-1-acetoxy-4-chloro-2-cyclohexene[146] (130 mg, 0.73 mmol) in DMF (4 mL) was added. The solution was stirred for 24 h at 23ºC, after which the reaction was quenched by addition of water at 0ºC and submitted to usual extractive work-up (Et_2O/H_2O). The crude mixture was purified by column chromatography (15:1 hexane-EtOAc) to yield **188** as a colorless oil (300 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (d, *J* = 10.2 Hz, 1H), 5.80 (m, 1H), 5.14 (s, 1H); 4.71 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 2.88 (m, 1H), 2.63 (t, *J* = 6.4 Hz, 2H), 2.02 (s, 3H), 1.92 (m, 1H), 1.72 (s, 2H), 1.69-1.62 (m, 1H), 1.65 (s, 3H), 1.59-1.41 (m, 8H), 1.38-1.24 (m, 6H), 0.98-0.76 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.31, 170.90, 170.63, 139.29, 134.95, 124.91, 112.37, 65.87, 61.05, 52.18, 51.86, 38.89, 31.41, 29.11 ($^3J(^{119}$Sn-C) = 20 Hz), 27.93, 27.39 ($^2J(^{119}$Sn-C) = 54 Hz), 26.23, 21.32, 19.14, 15.51, 13.68, 9.77 ($^1J(^{119}$Sn-C) = 316, (^{117}Sn-C) = 297 Hz). Anal. Calcd for $C_{30}H_{52}O_6Sn$: C, 57.43; H, 8.09. Found: C, 56.61; H, 5.29. HRMS-ESI Calcd for $C_{30}H_{52}O_6Na^{120}Sn$ $[M+Na]^+$: 651.2684. Found: 651.2688.

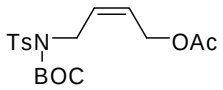
Dimethyl 2-(*trans*-4-Acetoxycyclohex-2-en-1-yl)-2-((*Z*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (189).



This compound was obtained by alkylation of 2-[(*Z*)-3-methyl-4-tributylstannyl-2-butenyl]malonate with *cis*-1-acetoxy-4-chloro-2-cyclohexene following the procedure

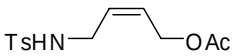
described for compound **191**. The product was obtained as acolorless oil (80%) after column chromatography (15:1 hexane-EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (dd, *J* = 10.2, 2.3 Hz, 1H), 5.66 (d, *J* = 10.5 Hz, 1H), 5.28 (m, 1H); 4.69 (t, *J* = 6.7 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 2.98 (m, 1H), 2.59 (m, 2H), 2.18-2.09 (m, 1H), 2.06 (s, 3H), 1.92-1.83 (m, 1H), 1.71 (s, 2H), 1.65 (s, 3H), 1.56-1.42 (m, 8H), 1.37-1.26 (m, 6H), 0.96-0.77 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.28, 170.83, 139.36, 132.15, 127.94, 112.27, 69.85, 61.13, 52.18, 52.01, 38.66, 31.35, 29.10 (^{3}J(^{119}Sn-C) = 20 Hz), 28.49, 27.39 (^{2}J(^{119}Sn-C) = 57 Hz), 26.26, 22.59, 21.34, 15.54, 13.69, 9.77 (^{1}J(^{119}Sn-C) = 314, (^{117}Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{30}H_{52}O_6Na^{120}Sn$ $[M+Na]^+$: 651.2684. Found: 651.2689.

(*Z*)-4-(*N*-(*tert*-Butoxycarbonyl)-4-toluenesulfonamido)-2-butenyl Acetate (193).



N-tert-butoxycarbonyl-(4-toluene)-sulfonamide (**192**)[168] (700 mg, 2.57 mmol) was alkylated with (*Z*)-1-acetoxy-4-bromo-2-butene (493 mg, 2.57 mmol) following the general alkylation procedure to afford **193** (370 mg, 38%) after column chromatography (4:1 hexane-EtOAc) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.77 (m, 2H), 4.79 (d, *J* = 4.7 Hz, 2H), 4.54 (d, *J* = 4.9, 2H), 2.54 (s, 3H), 2.09 (s, 3H), 1.35 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.80, 150.69, 144.24, 137.18, 129.53, 129.26, 127.98, 127.16, 84.53, 60.06, 43.57, 30.17, 27.87, 21.61, 20.93. HRMS-ESI Calcd for $C_{18}H_{25}NO_6SNa$ $[M+Na]^+$: 406.1300. Found: 406.1298.

(*Z*)-(4-Toluenesulfonamido)-2-butenyl Acetate (194).

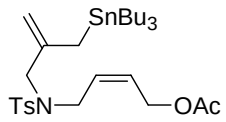


To a solution of **193** (340 mg, 0.88 mmol) in CH_2Cl_2 (7 mL) was added TFA (0.27 mL, 3.50 mmol) at 0ºC. The reaction mixture was stirred for 3 h. After extractive work-up (EtOAc/$NaHCO_3$ (5%)), the crude material was purified by column chromatography (3:1 to 1:1 hexane-EtOAc) to yield **194** as a colorless oil (240 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 9.1 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 5.67-5.56 (m, 2H), 4.88 (bs, 1H), 4.52 (d, *J* = 5.5 Hz, 2H), 3.67 (t, *J* = 5.8 Hz, 2H), 2.45

168 Henry, J. R.; Marcin, L. R.; Mcintosh, M. C.; Scola, P. M.; Harris, G. D. Jr. *Tetrahedorn Lett.* **1989**, *30*, 5709-5712.

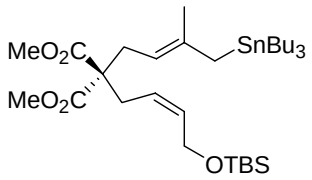
(s, 3H), 2.05 (s, 3H).[13]C NMR (100 MHz, $CDCl_3$) δ 170.95, 143.55, 136.86, 129.76, 129.97, 127.26, 127.17, 59.58, 39.89, 21.54, 20.91. HRMS-ESI Calcd for $C_{13}H_{17}NO_4SNa$ $[M+Na]^+$: 306.0776. Found: 306.0768.

(*Z*)-4-[*N*-((2-Methyltri-*n*-butylstannyl)-2-propenyl)-4-toluenesulfonamido]-2-butenyl Acetate (195).



Compund **194** (210 mg, 0.56 mmol) was alkylated with 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene[169] (160 mg, 0.56 mmol) according to the general alkylation procedure. The crude mixture was purified by column chromatography (6:1 hexane-EtOAc) to yield **195** (195 mg, 56%) as a colorless oil. [1]H NMR (400 MHz, CD_2Cl_2) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 5.60 (dtt, *J* = 11.1, 6.7, 1.6 Hz, 1H), 5.45 (dtt, *J* = 11.1, 6.7, 1.4 Hz, 1H), 4.71 (s, $^4J(^{119}$Sn-H) = 18.2 Hz, 1H), 4.64 (d, *J* = 1.5, $^4J(^{119}$Sn-H) = 18.1 Hz, 1H), 4.56 (d, *J* = 6.7 Hz, 2H), 3.88 (d, *J* = 6.7 Hz, 2H), 3.59 (s, 2H), 2.46 (s, 3H), 2.05 (s, 3H), 1.80 (s, 2H), 1.58-1.44 (m, 6H), 1.41-1.27 (m, 6H), 1.04-0.83 (m, 15H). [13]C NMR (100 MHz, CD_2Cl_2) δ 170. 44, 144.54, 143.48, 137.11, 129.67, 128.99, 127.14, 126.84, 108.84, 59.67, 43.80, 29.03 ($^3J(^{119}$Sn-C) = 20 Hz), 27.39 ($^2J(^{119}$Sn-C) = 56 Hz), 21.22, 20.60, 15.14, 13.45, 9.40 ($^1J(^{119}$Sn-C) = 319, (^{117}Sn-C) = 307 Hz). HRMS-ESI Calcd for $C_{29}H_{49}NO_4SNa^{120}Sn$ $[M+Na]^+$: 650.2302. Found: 650.2293.

Dimethyl [2-((*Z*)-4-*tert*-Butyldimethylsiloxy-2-butenyl)-2-((*E*)-3-methyl-4-tri-n-butylstannyl-2-butenyl)]malonate (177).



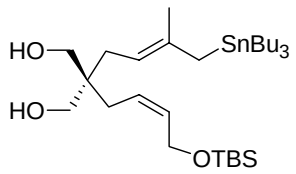
This compound was obtained by alkylation of **185** with (*Z*)-1-bromo-4-*tert*-butyldimethylsiloxy-2-butene[170] following the general alkylation procedure. Purification by column chromatography (30:1 hexane-EtOAc) yielded the title product as a colorless oil (82%). [1]H NMR (400 MHz, CD_2Cl_2) δ 5.64 (dtt, *J* = 11.1, 6.1, 1.5 Hz, 1H), 5.40-

169 Keck, G. E.; Yu, T.; McLaws, M. D. *J. Org. Chem*. **2005**, *70*, 2543-2550.

170 Sun, M.; Deng, Y.; Batyreva, E.; Sha, W.; Salomon, R. G. *J. Org. Chem*. **2002**, *67*, 3575-3584.

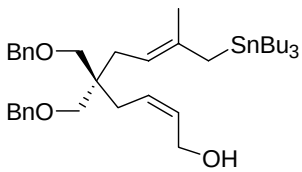
5.27 (m, 1H), 4.79 (t, *J* = 7.6 Hz, 1H), 4.23 (dd, *J* = 6.1, 1.7 Hz, 2H), 3.70 (s, 6H), 2.63 (d, *J* = 6.7 Hz, 2H), 2.61 (d, *J* = 7.3 Hz, 2H), 1.78 (s, 2H), 1.62 (s, 3H), 1.56-1.45 (m, 6H), 1.39-1.28 (m, 6H), 0.98-0.77 (m, 24H), 0.10 (s, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 171.46, 139.86, 133.43, 123.72, 112.57, 59.23, 57.75, 52.17, 31.30, 30.33, 29.09 ($^3J(^{119}$Sn-C) = 20 Hz), 27.38 ($^2J(^{119}$Sn-C) = 54 Hz), 25.65, 22.39, 18.47, 18.13, 13.45, 9.37 ($^1J(^{119}$Sn-C) = 313, (^{117}Sn-C) = 299 Hz), -5.51. HRMS-ESI Calcd for $C_{32}H_{62}O_5SiNa^{120}Sn$ $[M+Na]^+$: 697.3286. Found: 697.3275.

2-((*Z*)-4-*tert*-Butyldimethylsiloxy-2-butenyl)-2-((*E*)-3-methyl-4-tri-n-butylstannyl-2-butenyl)-1,3-propanediol (196).



To a suspension of $LiAlH_4$ (31 mg, 0.82 mmol), in Et_2O (5 mL) at 0ºC was slowly added a solution of **177** (390 mg, 0.59 mmol) in Et_2O (5 mL). The reaction was stirred from 0ºC to 23ºC for 1 h then was cooled to 0ºC and quenched by addition of a saturated solution of NH_4Cl. After usual extractive work-up (Et_2O/water) and purification by column chromatography (1:1 hexane-EtOAc) the product was obtained as a colorless oil (154 mg, 42%).^{1}H NMR (400 MHz, CD_2Cl_2) δ 5.82-5.65 (m, 2H), 5.05 (td, *J* = 7.6, 1.2 Hz, 1H), 4.25 (d, *J* = 6.7 Hz, 2H), 3.53 (s, 2H), 3.52 (s, 2H), 2.95 (t, *J* = 6.1 Hz, 2H), 2.24 (d, *J* = 7.9, 2H), 1.90 (d, *J* = 7.9, 2H), 1.81 (s, 2H), 1.64 (s, 3H), 1.57-1.46 (m, 6H), 1.40-1.29 (m, 6H), 0.97-0.85 (m, 24H), 0.13 (s, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 138.10, 130.04, 129.59, 114.31, 68.13, 58.36, 43.57, 30.18, 29.13 ($^3J(^{119}$Sn-C) = 20 Hz), 28.19, 27.41 ($^2J(^{119}$Sn-C) = 55 Hz), 25.62, 22.43, 18.41, 18.20, 13.45, 9.43 ($^1J(^{119}$Sn-C) = 312, (^{117}Sn-C) = 298 Hz), -5.51. HRMS-ESI Calcd for $C_{30}H_{62}O_3SiNa^{120}Sn$ $[M+Na]^+$: 641.3388. Found: 641.3400.

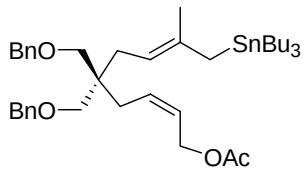
(2*E*,7*Z*)-9-Hidroxy-5,5-bis(benzyloxymethyl)-1-(tri-n-butylstannyl)-8-methyl-2,7-nonadiene (197).



To a suspension of NaH (60% in mineral oil, 23 mg, 0.57 mmol) in DMF (3 mL) was added **196** (120 mg, 0.19 mmol) dissolved in DMF (2 mL) at 0ºC. After stirring for

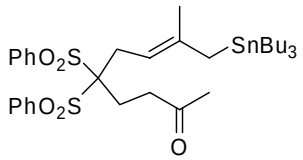
10 min benzylbromide (0.17 mL, 1.17 mmol) was added. The reaction mixture was stirred at 23ºC for 16 h then was quenched by addition of water and submitted to usual extractive work-up (Et_2O/H_2O/brine). The reaction mixture was dissolved in THF (5 mL) cooled to 0ºC and treated with TBAF (1 M, 0.19 mL) for 1 h. After extractive work-up (Et_2O/H_2O) and purification by column chromatography (15:1 hexane-EtOAc) **197** was obtained as a colorless oil (59 mg, 44%). Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.25 (m, 10H), 5.83-5.74 (m, 1H), 5.67-5.56 (m, 1H), 4.99 (t, *J* = 7.9 Hz, 1H), 4.49 (s, 4H), 4.13 (t, *J* = 6.7 Hz, 2H), 3.32 (s, 4H), 2.16 (d, *J* = 7.9 Hz, 2H), 2.06 (d, *J* = 7.6 Hz, 2H), 1.99 (t, *J* = 3.8 Hz, 1H), 1.75 (s, 2H), 1.60 (s, 3H), 1.54-1.41 (m, 6H), 1.37-1.26 (m, 6H), 0.96-0.75 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.57, 138.07, 130.78, 128.76, 128.28, 127.51, 127.45, 114.74, 73.38, 72.26, 58.16, 43.22, 30.26, 29.55, 29.17 ($^3J(^{119}$Sn-C) = 20 Hz), 27.42 ($^2J(^{119}$Sn-C) = 52 Hz), 22.55, 18.64, 13.73, 9.53 ($^1J(^{119}$Sn-C) = 311, (^{117}Sn-C) = 296 Hz). HRMS-ESI Calcd for $C_{38}H_{60}O_3Na^{120}Sn$ $[M+Na]^+$: 707.3462. Found: 707.3479.

(2*E*,7*Z*)-9-Acetoxy-5,5-bis(benzyloxymethyl)-1-(tri-*n*-butylstannyl)-8-methyl-2,7-nonadiene (198).



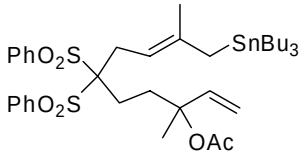
To a solution of **197** (54 mg, 0.078 mmol) and DMAP (3 mg, 0.024 mmol) in CH_2Cl_2 (3 mL) at 0ºC was added *i*-$PrEt_2N$ (0.03 mL, 0.15 mmol), and Ac_2O (0.01 mL, 0.15 mmol). The resulting mixture was stirred at 23ºC overnight. After extractive workup (CH_2Cl_2/H_2O) and chromatography (10:1 hexane-EtOAc), **198** was obtained as a colorless oil (52 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 10H), 5.76-5.58 (m, 2H), 4.99 (t, *J* = 7.9 Hz, 1H), 4.66 (d, *J* = 6.4 Hz, 2H), 4.84 (s, 4H), 3.30 (s, 2H), 3.29 (s, 2H), 2.19 (d, *J* = 7.6 Hz, 2H), 2.07 (d, d, *J* = 7.6 Hz, 2H), 2.04 (s, 3H), 1.76 (s, 2H), 1.58 (s, 3H), 1.54-1.43 (m, 6H), 1.37-1.25 (m, 6H), 0.96-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.94, 138.86, 137.84, 130.72, 128.22, 127.36, 127.30, 125.63, 114.91, 73.21, 72.40, 60.64, 43.13, 30.59, 30.16, 29.17 ($^3J(^{119}$Sn-C) = 20 Hz), 27.42 ($^2J(^{119}$Sn-C) = 54 Hz), 22.56, 20.98, 18.62, 13.73, 9.53 ($^1J(^{119}$Sn-C) = 311, (^{117}Sn-C) = 297 Hz). HRMS-ESI Calcd for $C_{40}H_{62}O_4Na^{120}Sn$ $[M+Na]^+$: 749.3568. Found: 749.3565.

(2*E*)-5,5-Bis(phenylsulfonyl)-8-methyl-9-(tri-*n*-butylstannyl)-7-nonen-2-ona (199).[107]



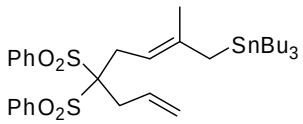
A solution of **139** (700 mg, 1.07 mmol), methyl vinyl ketone (0.1 mL, 1.28 mmol) and $[RuH_2(PPh_3)_4]$ (240 mg, 0.21 mmol) in MeCN (16 mL) was stirred at 23 ºC for 12 h. The solvent was removed and the crude mixture was purified by column chromatogragphy (4:1 hexane-EtOAc) to yield **199** (86%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.00 (m, 4H), 7.76-7.68 (m, 2H), 7.64-7.56 (m, 4H), 4.95 (bt, *J* = 6.1 Hz, 1H), 3.04-2.95 (m, 2H), 2.81 (d, *J* = 6.4 Hz, 2H), 2.54-2.47 (m, 2H), 2.15 (s, 3H), 1.72 (s, 2H), 1.53-1.42 (m, 9H), 1.37-1.25 (m, 6H), 0.96-0.74 (m, 15H).

(2*E*)-8-Acetoxy-5,5bis(phenylsulfonyl)-2,8-dimethyl-1-(tri-*n*-butylstannyl)-2,9-decadiene (200).[107]



To a solution of **300** (642 mg, 0.88 mmol) in THF (20 mL) was slowly added vinylmagnesium bromide (1.3 mL, 1 M in THF) at 0 °C. The mixture was stirred at 23 °C for 2 h, after which the reaction was quenched by addition of water (5 mL). After the extractive workup (Et_2O/H_2O) the remaining oil was treated with Ac_2O (0.187 mL, 2.67 mmol), DMAP (417 mg, 3.6 mmol) and *i*-Pr_2NEt (0.461 mL, 2.67 mmol) following the general acetylation procedure. After purification by column chromatography (2:1 hexane-EtOAc) the title product was obtained as a colorless oil (463 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.03 (m, 4H), 7.75-7.66 (m, 2H), 7.62-7.52 (m, 4H), 5.92 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.16 (d, *J* = 10.8 Hz, 1H), 5.15 (d, *J* = 17.6 Hz, 1H), 5.05 (t, *J* = 5.8 Hz, 1H), 2.90 (d, *J* = 5.8 Hz, 2H), 2.35-2.07 (m, 4H), 1.98 (s, 3H), 1.77 (s, 2H), 1.62-1.43 (m, 12H), 1.39-1.23 (m, 6H), 1.00-078 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.56, 140.99, 140.81, 136.84, 134.34, 131.45, 128.33, 114.01, 109.59, 91.61, 82.26, 34.14, 29.13 ($^3J(^{119}$Sn-C) = 20 Hz), 27.38 ($^2J(^{119}$Sn-C) = 54Hz), 26.99, 23.57, 22.82, 22.41, 22.10, 18.95, 13.75, 9.63 ($^1J(^{119}$Sn-C) = 314, (^{117}Sn-C) = 302 Hz).

(2*E*)-5,5-Bis(phenylsulfonyl)-1-(tri-*n*-butylstannyl)-2-methyl-2,7-nonadiene (176).



This compound was prepared by alkylation of **139** with allyl chloride following the general alkylation procedure. The crude material was purified by column chromatography (10:1 hexane-EtOAc) to yield **176** as a vitreous solid (78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-7.99 (m, 4H), 7.76-7.63 (m, 2H), 7.59-7.51 (m, 4H), 5.97 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.20 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.16 (dd, *J* = 16.9, 1.4 Hz, 1H), 5.13 (overlapping t, *J* = 6.7 Hz, 1H), 3.01 (d, *J* = 6.7 Hz, 2H), 2.93 (d, *J* = 6.4 Hz, 2H), 1.76 (s, 2H), 1.57-1.40 (m, 9H), 1.35-1.24 (m, 6H), 0.97-074 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.92, 136.98, 134.37, 131.51, 130.37, 128.36, 119.86, 109.86, 91.09, 32.79, 29.12 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.93, 27.39 ($^{2}J(^{119}$Sn-C) = 54Hz), 22.75, 18.98, 13.72, 9.60 ($^{1}J(^{119}$Sn-C) = 314, (^{117}Sn-C) = 300 Hz). HRMS-ESI Cald for $C_{33}H_{50}O_4Na^{116}SnS_2$ $[M+Na]^+$: 713.2066. Found: 713.2095.

General cyclization procedures:

General procedure for cyclizations catalyzed by $[RhCl(PPh_3)_3]$

To a solution of $[RhCl(PPh_3)_3]$ (6.5 μmol) and LiCl (0.32 mmol) in DMF (2 mL) the corresponding allylstannane-allylacetate (0.065 mmol) in DMF (0.5 mL) was added. The reaction was stirred at 80ºC for 14 h, and was then cooled to 23ºC. To remove the tin residues[171] the mixture was treated with aqueous NaOH (1M, 5 mL) at 23ºC for 5 h. After usual extractive work-up (Et_2O/H_2O) the crude material was purified by column chromatography.

General procedure for cyclizations catalyzed by $[RhCl(CO)_2]_2$

To a solution of $[RhCl(CO)_2]_2$ (3.2 μmol), 2-dicyclohexilphosphino-2',4',6'-triisopropylbiphenyl (6.5 μmol) and *di*-isopropylamine (0.195 mmol) in toluene (2 mL) the corresponding allylstannane-allylacetate (0.065 mmol) dissolved in toluene (0.5 mL) was added. The reaction was stirred at 80ºC for 14 h, and was then cooled to 23ºC. To remove the tin residues[171] the mixture was treated with aqueous NaOH (1M, 5 mL) at

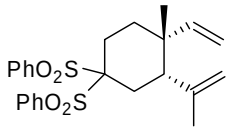
171 Renaud, P.; Lacôte, E.; Quaranta, L. *Tetrahedron Lett*. **1998**, *39*, 2123-2126.

23ºC for 5 h. After usual extractive work-up (CH_2Cl_2/H_2O) the crude material was purified by column chromatography.

General procedure for cyclizations catalyzed by cationic complex 260

To a solution of **165** (1.9 μmol), in DCE (2 mL) at the indicated temperature the corresponding allylstannane-allylacetate (0.063 mmol) in DCE (0.5 mL) was added. The reaction was stirred at the same temperature for the time indicated and was then cooled to 23ºC. To remove the tin residues[171] the mixture was treated with aqueous NaOH (1M, 5 mL) at 23ºC for 5 h. After usual extractive work-up (CH_2Cl_2/H_2O) the crude material was purified by column chromatography.

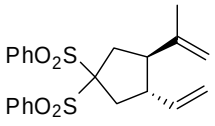
(3R*,4S*)-1,1-Bis(phenylsulfonyl)-4-ethenyl-4-methyl-3-(methylethenyl) cyclohexane (89b).



White solid.[1]H NMR (400 MHZ, $CDCl_3$) δ 8.12-8.06 (m, 2H), 8.05-7.99 (m, 2H), 7.75-7.67 (m, 2H), 7.64-7.55 (m, 4H), 6.12 (dd, *J* = 17.2, 11.1 Hz, 1H), 5.03 (dd, *J* = 11.1, 1.2 Hz, 1H), 5.00 (dd, *J* = 17.5, 1.3 Hz, 1H), 4.86 (br s, 1H), 4.74 (br s, 1H), 2.86 (dd, *J* = 13.7, 3.2 Hz, 1H), 2.71 (t, *J* = 15.1 Hz, 1H), 2.58 (ddd, *J* = 15.6, 14.0, 5.2 Hz, 1H), 2.31-2.10 (m, 2H), 2.05 (dt, *J* = 15.0, 1.8 Hz, 1H), 1.67 (s, 3H), 1.60 (ddd, *J* = 13.6, 5.2, 2.8 Hz, 1H), 1.07 (s, 3H). [13]C NMR (100 MHz, $CDCl_3$) δ 144.84, 140.22, 136.28, 136.18, 134.48, 134.32, 131.57, 131.12, 128.52, 128.47, 114.31, 114.25, 88.37, 48.68, 38.00, 36.55, 27.46, 26.30, 23.04, 22.38.

[1]H NMR significative signals of *trans*-isomer (**89a**): [1]H NMR (400 MHZ, $CDCl_3$) δ 5.82 (dd, *J* = 17.2, 10.8 Hz, 1H), 4.94 (dd, *J* = 9.3, 1.2 Hz, 1H), 4.90 (m, 1H), 4.86 (br s, 1H), 4.64 (br s, 1H), 1.71 (s, 3H), 0.94 (s, 3H).

***trans*-1,1-Bis(phenylsulfonyl)-3-ethenyl-4-(1-methylethenyl)cyclopentane (106a).**[172]

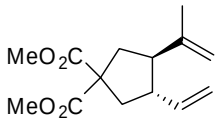


172 Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 3620-3628.

^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.16-8.05 (m, 4H), 7.80-7.72 (m, 2H), 7.68-7.60 (m, 4H), 5.56 (ddd, *J* = 17.8, 10.5, 7.3 Hz, 1H), 5.04 (d, *J* = 10.5 Hz, 1H), 5.00 (d, *J* = 17.8 Hz, 1H), 4.83 (s, 1H), 4.72 (s, 1H), 2.72 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.67 (dd, *J* = 14.9, 7.3 Hz, 1H), 2.60-2.30 (m, 4H), 1.65 (s, 3H).

^{1}H NMR significative signals of *cis*-isomer (**106b**): ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.67 (dt, *J* = 16.9, 9.6 Hz, 1H), 4.99 (dd, *J* = 16.9, 1.5 Hz, 1H), 4.94 (d, *J* = 9.9, 1.5 Hz, 1H), 4.65 (s, 1H), 3.15-3.04 (m, 2H), 3.03-2.83 (m, 2H), 1.68 (s, 3H).

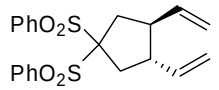
Dimethyl 4-Ethenyl-3-(2-methylethenyl)cyclopentane-1,1-dicarboxylate (179a).



Purified by column chromatography (10:1 hexane-EtOAc). Obtained as 90:10 and 88:12 mixture of *trans*/*cis* isomers. Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.66 (ddd, *J* = 17.5, 10.2, 7.3 Hz, 1H), 5.04 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.00 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.80 (q, *J* = 1.5 Hz, 1H), 4.78 (br s, 1H), 3.76 (s, 6H), 2.62-2.49 (m, 3H), 2.44-2.36 (m, 1H), 2.13 (dd, *J* = 13.4, 11.4 Hz, 1H), 2.09-1.99 (m, 1H), 1.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.99, 172.97, 144.30, 139.46, 115.19, 111.87, 57.92, 52.84, 47.23, 40.20, 39.26, 19.54. HRMS-ESI Calcd for $C_{14}H_{20}O_4Na$ $[M + Na]^+$: 275.1259. Found: 275.1248.

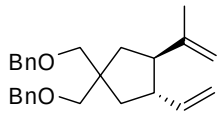
^{13}C NMR significative signals of *cis*-isomer (**179b**): ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.10, 114.82, 110.62, 58.56, 49.28, 44.79, 39.22, 36.38.

1,1-Bis(phenylsulfonyl)-3,4-diethenylcyclopentane (201).[172]



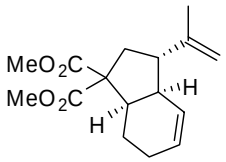
Obtained as a 87:13 mixture of *trans*/*cis* isomers: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.14-8.05 (m, 4H), 7.79-7.70 (m, 2H), 7.67-7.58 (m, 4H), 5.60 (ddd, *J* = 17.2, 10.2, 7.0 Hz, 2H), 5.06 (dd, *J* = 10.3, 1.5 Hz, 2H), 5.01 (d, *J* = 17.2 Hz, 2H), 2.73 (dd, *J* = 14.3, 5.8 Hz, 2H), 2.50-2.28 (m, 4H).

***trans*-1,1-Bis(benzyloxymethyl)-3-ethenyl-4-(1-methylethenyl)cyclopentane (206).**



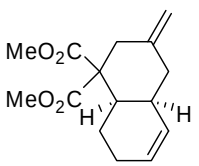
Purified by column chromatography (100:1 hexane-EtOAc). Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.38-7.26 (m, 10H), 5.67 (ddd, *J* = 17.2, 10.2, 7.3 Hz, 1H), 5.03-4.91 (m, 2H), 4.77-4.74 (m, 1H), 4.73 (s, 1H), 4.55 (s, 4H), 3.40 (s, 4H), 2.48 (ddd, *J* = 18.1, 11.1, 7.6 Hz, 1H), 2.31 (ddd, *J* = 19.0, 11.4, 7.6 Hz, 1H), 1.89 (dd, *J* = 13.1, 7.3 Hz, 1H), 1.83 (dd, *J* = 13.4, 7.6 Hz, 1H), 1.68 (s, 3H), 1.46 (dd, *J* = 13.1, 11.7 Hz, 1H), 1.38 (dd, *J* = 13.1, 11.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 146.08 (C), 141.24 (CH), 138.89 (C), 128.27 (CH), 127.38 (CH), 127.36 (CH), 113.90 (CH_2), 110.61 (CH_2), 75.15 (CH_2), 75.04 (CH_2), 73.20 (CH_2), 52.75 (CH), 46.91 (CH), 45.44 (C), 39.36 (CH_2), 38.39 (CH_2), 19.71 (CH_3). HRMS-ESI Calcd for $C_{26}H_{32}O_2$ $[M+Na]^+$: 399.2300. Found: 399.2284. The relative stereochemistry was determined according to COSY, HMQC, HMBC and NOESY experiments.

(3*R,3a*S**,7a*S**)-Dimethyl 3-(Prop-1-en-2-yl)-3,3a,7,7a-tetrahydro-1*H*-indene-1,1(2H,6H)-dicarboxylate (202).**



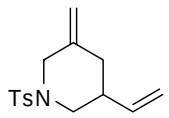
Purified by column chromatography (10:1 hexane-EtOAc). Colorless oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.73 (dt, *J* = 9.9, 3.8 Hz, 1H), 5.66 (m, 1H), 4.77 (m, 2H), 3.74 (s, 6H), 2.96 (ddd, *J* = 13.4, 10.2, 4.1 Hz, 1H), 2.86 (dd, *J* = 14.3, 8.8 Hz, 1H), 2.62-2.48 (m, 2H), 2.11-2.03 (m, 2H), 1.85 (dd, *J* = 14.6, 8.8 Hz, 1H), 1.69 (s, 3H), 1.41 (ddd, *J* = 12.2, 7.6, 4.1 Hz, 1H), 1.36-1.22 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 173.18 (C), 171.07 (C), 144.94 (C), 127.58 (CH), 126.63 (CH), 111.04 (CH_2), 63.19 (C), 52.65 (CH_3), 52.24 (CH_3), 52.08 (CH), 43.33 (CH), 42.86 (CH), 37.89 (CH_2), 25.05 (CH_2), 21.58 (CH_2), 19.51 (CH_3). HRMS-ESI Calcd for $C_{16}H_{22}O_4Na$ $[M+Na]^+$: 301.1416. Found: 301.1405. The relative stereochemistry was determined according to COSY, HMQC, HMBC and NOESY experiments.

(4a*R,8a*S**)-Dimethyl 3-methylene-2,3,4,4a,8,8a-hexahydronaphthalene-1,1(7*H*)-dicarboxylate (203).**



Purified by column chromatography (10:1 hexane-EtOAc). Colorless oil. ^{1}H NMR (400 MHZ, C_6D_6) δ 5.68 (m, 1H), 5.62 (m, 1H), 4.84 (q, *J* = 1.7 Hz, 1H), 4.81 (q, *J* = 1.5 Hz, 1H), 3.45 (s, 3H), 3.39 (s, 3H), 3.14, 2.90 (AB system, J_{AB} = 13.7 Hz, 2H), 3.10-2.97 (m, 2H), 2.23 (ddd, *J* = 13.1, 4.7, 1.7 Hz, 1H), 2.12-1.92 (m, 3H), 1.68 (dq, *J* = 12.8, 5.8 Hz, 1H), 1.29 (dd, *J* = 12.5, 5.5 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 171.21 (C), 170.86 (C), 143.93 (C), 131.04 (CH), 125.62 (CH), 109.86 (CH_2), 61.10 (C), 52.58 (CH_3), 52.46 (CH_3), 37.29 (CH_2), 37.27 (CH), 35.77 (CH), 35.48 (CH_2), 26.13 (CH_2), 19.81 (CH_2). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.89; H, 7.31. HRMS-ESI Calcd for $C_{15}H_{20}O_4Na$ $[M+Na]^+$: 287.1259. Found: 287.1252. The relative stereochemistry was determined according to COSY, HMQC, HMBC and NOESY experiments.

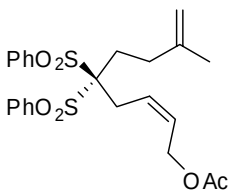
3-Methylene-1-tosyl-5-vinylpiperidine (204).



Purified by column chromatography (8:1 hexane-EtOAc). Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 5.69 (ddd, *J* = 17.2, 10.5, 6.4 Hz, 1H), 5.10 (dt, *J* = 17.2, 1.2 Hz, 1H), 5.07 (dt, *J* = 10.2, 1.2 Hz, 1H), 4.96 (d, *J* = 1.2 Hz, 1H), 4.88 (s,1H), 4.02 (d, *J* = 12.6 Hz, 1H), 3.67 (m, 1H), 3.02 (d, *J* = 12.3 Hz, 1H), 2.46 (s, 3H), 2.43-2.27 (m, 3H), 1.87 (t, *J* = 12.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 143.56 (C), 139.43 (C), 138.41 (CH), 129.67 (CH), 127.93 (CH), 115.72 (CH_2), 112.50 (CH_2), 51.97 (CH_2), 50.58 (CH_2), 40.09 (CH), 37.79 (CH_2), 21.56 (CH_3). Anal. Calcd for $C_{15}H_{19}NO_2S$: C, 64.95; H, 6.90; S, 11.56; N, 5.05. Found: C, 64.57; H, 6.76; S, 11.31; N, 5.03. HRMS-ESI Calcd for $C_{15}H_{19}NO_2NaS$ [M + Na]$^+$: 300.1034. Found: 300.1020.

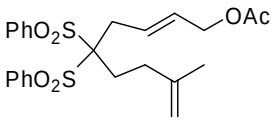
Destannylated products:

(2*Z*)-5,5-Bis(phenylsulfonyl)-8-methyl-2,8-nonadiene Acetate (168).



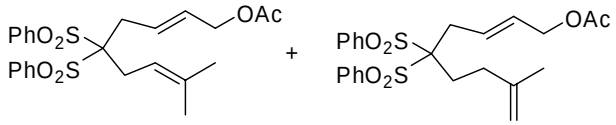
Colorless oil:^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.12-8.00 (m, 4H), 7.76-7.68 (m, 2H), 7.65-7.55 (m, 4H), 5.94 (dtt, *J* = 11.1, 6.1, 1.5 Hz, 1H), 5.70 (dtt, *J* = 11.1, 6.4, 2.0 Hz, 1H), 4.74 (br s, 1H), 4.65 (br s, 1H), 4.56 (d, *J* = 7.6 Hz, 2H), 3.07 (d, *J* = 6.1 Hz, 2H), 2.34 (s, 4H), 2.07 (s, 3H), 1.70 (s, 3H).

(2*E*)-5,5-Bis(phenylsulfonyl)-8-methyl-2,8-nonadiene Acetate (169).



Colorless oil:^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.03-7.94 (m, 4H), 7.69-7.61 (m, 2H), 7.56-7.49 (m, 4H), 5.88 (dtt, *J* = 15.5, 6.7, 1.2 Hz, 1H), 5.68 (dtt, *J* = 15.2, 6.1, 1.5 Hz, 1H), 4.66 (br s, 1H), 4.57 (br s, 1H), 4.47 (dd, *J* = 6.1, 1.0 Hz, 2H), 3.00 (dd, *J* = 6.7, 1.1 Hz, 2H), 2.34-2.27 (m, 2H), 2.23 (ddd, *J* = 8.7, 4.6, 2.0 Hz, 2H), 2.00 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.63, 143.97, 136.77, 134.66, 131.38, 130.14, 128.63, 126.70, 110.96, 90.81, 64.28, 64.28, 31.81, 31.02, 27.63, 22.49, 20.89. HRMS-ESI Calcd for $C_{24}H_{28}O_6NaS_2$ $[M+Na]^+$: 499.1225. Found: 499.1203.

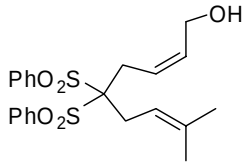
(*E*)-5,5-Bis(phenylsulfonyl)-8-methyl-2,7-nonadiene Acetate (171a) and (*E*)-5,5-bis(phenylsulfonyl)-8-methyl-2,8-nonadiene Acetate (171b).



171a **171b**

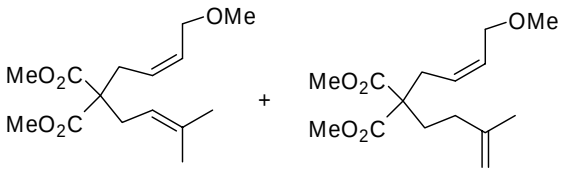
Colorless oil, 1:1 mixture:^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.12-8.03 (m, 8H, A and B), 7.78-7.69 (m, 4H, A and B), 7.67-7.56 (m, 8H, A and B), 6.03-5.89 (m, 2H, A and B), 5.83-5.64 (m, 2H, A and B), 5.33 (t, *J* = 6.4 Hz, 1H, A), 4.76 (s, 1H, B), 4.67 (s, 1H, B), 4.60-4.51 (m, 4H, A and B), 3.09 (d, *J* = 6.7 Hz, 2H, B), 3.04 (d, *J* = 6.4 Hz, 2H, A), 2.94 (d, *J* = 6.2 Hz, 2H, A), 2.45-2.37 (m, 2H, B), 2.37-2.29 (m, 2H, B), 2.09 (s, 6H, A and B), 1.73 (s, 3H, A), 1.71 (s, 3H, A), 1.55 (s, 3H, B). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.67, 143.97, 136.87, 136.78, 136.71, 134.66, 134.53, 131.51, 131.39, 130.15, 129.60, 128.63, 128.48, 126.83, 126.71, 115.09, 110.96, 90.82, 90.52, 64.41, 64.29, 31.96, 31.81, 31.03, 28.15, 27.63, 26.04, 22.50, 20.94, 20.89, 18.12. HRMS-ESI Calcd for $C_{24}H_{28}O_6NaS_2$ $[M+Na]^+$: 499.1225. Found: 499.1223.

(*Z*)-5,5-Bis(phenylsulfonyl)-8-methyl-2,7-nonadien-1-ol (173).



Colorles oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.10-8.02 (m, 4H), 7.77-7.69 (m, 2H), 7.64-7.55 (m, 4H), 5.87-5.79 (m, 1H), 5.79-5.71 (m, 1H), 5.28 (tt, *J* = 6.4, 1.5 Hz, 1H), 4.17 (t, *J* = 4.7 Hz, 2H), 3.06 (d, *J* = 6.4 Hz, 2H), 2.97 (d, *J* = 6.1 Hz, 2H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.66 (t, *J* = 5.2 Hz, 1H), 1.56 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.99, 136.80, 134.57, 132.58, 131.43, 128.52, 123.34, 115.11, 90.95, 58.46, 28.06, 27.11, 26.04, 18.18. HRMS-ESI Calcd for $C_{22}H_{26}O_5NaS_2$ $[M+Na]^+$: 457.1198. Found: 457.1210.

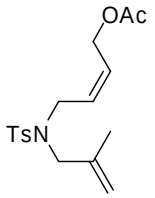
Dimethyl (*Z*)-2-(4-Methoxy-2-butenyl)-2-(3-methyl-2-butenyl)malonate (181a) and dimethyl (*Z*)-2-(4-methoxy-2-butenyl)-2-(3-methyl-3-butenyl)malonate (181b).



181a **181b**

Obtained as a 83:17 mixture; 274a major, 274b minor. Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.76-5.62 (m, 1H, major and minor), 5.50-5.39 (m, 1H, major and minor), 4.97 (t, *J* = 7.0, 1H, major), 4.74 (s, 1H, minor), 4.71 (s, 1H, minor), 3.99 (d, *J* = 6.1 Hz, 2H, minor), 3.97 (d, *J* = 6.7 Hz, 2H, major), 3.74 (s, 6H, minor), 3.73 (s, 6H, major), 3.35 (s, 3H, minor), 3.34 (s, 3H, major), 2.73 (d, *J* = 7.9 Hz, 2H, minor), 2.67 (d, *J* = 7.6 Hz, 2H, major), 2.63 (d, *J* = 7.3 Hz, 2H, major), 2.09-2.01 (m, 2H, minor), 1.94-1.85 (m, 2H, minor), 1.74 (S, 3H, minor), 1.72 (s, 3H, major), 1.59 (s, 3H, minor). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.55 (major and minor), 144.60 (minor), 135.97 (major), 130.19 (minor), 130.09 (major), 126.31 (major), 126.13 (minor), 117.41 (major), 110.43 (minor), 68.06 (major), 68.02 (minor), 58.09 (minor), 58.05 (major), 57.62 (major), 57.25 (minor), 52.45 (minor), 52.42 (major), 32.16 (minor), 31.13 (major), 30.79 (minor), 30.70 (minor), 30.53 (major), 29.70 (minor), 26.03 (major), 22.47 (minor), 17.89 (major). HRMS-ESI Calcd for $C_{15}H_{24}O_5Na$ $[M+Na]^+$: 307.1521. Found: 307.1519.

(*Z*)-4-(*N*-(2-methylallyl)-4-toluenesulfonamido)-2-butenyl Acetate (205).



Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.61 (dtt, *J* = 11.1, 6.7, 1.4 Hz, 1H), 5.43 (dtt, *J* = 11.1, 6.7, 1.4 Hz, 1H), 4.93 (s, 1H), 4.87 (s,1H), 4.55 (d, *J* = 7.0 Hz, 2H), 3.85 (d, *J* = 7.0 Hz, 2H), 3.70 (s, 2H), 2.45 (s, 3H), 2.06 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 170.80 (C), 143.29 (C), 140.33 (C), 137.08 (C), 129.72 (CH), 128.96 (CH), 127.22 (CH), 127.15 (CH), 114.61 (CH_2), 59.64 (CH_2), 53.57 (CH_2), 43.67 (CH_2), 21.52 (CH_3), 20.86 (CH_3), 19.79 (CH_3). HRMS-ESI Calcd for $C_{17}H_{23}NO_4NaS$ $[M+Na]^+$: 360.1245. Found: 360.1252.

Crystal data and structure refinement for complex 153.

Table 1. Crystal data and structure refinement for **153**.

Empirical formula	$C_{42}H_{40}BF_4FeP_2Rh$	
Formula weight	852.25	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	Cc	
Unit cell dimensions	a = 21.0978(17) Å	a= 90°.
	b = 11.0289(10) Å	b= 123.513(4)°.
	c = 18.6451(17) Å	g = 90°.
Volume	3617.2(5) Å^3	
Z	4	
Density (calculated)	1.565 Mg/m^3	
Absorption coefficient	0.998 mm^{-1}	
F(000)	1736	
Crystal size	0.30 x 0.10 x 0.10 mm^3	
Theta range for data collection	2.85 to 37.09°.	
Index ranges	-35<=h<=21, -18<=k<=10, -25<=l<=31	
Reflections collected	25054	
Independent reflections	12910 [R(int) = 0.0394]	

Completeness to theta = 37.09°	98.4 %
Absorption correction	SADABS (Bruker-Nonius)
Max. and min. transmission	0.9068 and 0.7540
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12910 / 2 / 460
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0352, wR2 = 0.0862
R indices (all data)	R1 = 0.0388, wR2 = 0.0885
Absolute structure parameter	0.000(10)
Largest diff. peak and hole	2.041 and -3.057 e.Å^{-3}

Table 2. Bond lengths [Å] and angles [°] for **153**.

Rh(1)-C(35)	2.213(2)	C(2)-C(3)	1.388(4)
Rh(1)-C(36)	2.2179(19)	C(4)-C(3)	1.385(4)
Rh(1)-C(41)	2.256(3)	C(4)-C(5)	1.397(4)
Rh(1)-C(42)	2.272(2)	C(10)-C(11)	1.384(3)
Rh(1)-P(4)	2.3252(7)	C(10)-C(9)	1.402(3)
Rh(1)-P(3)	2.3658(5)	C(11)-C(12)	1.392(3)
Fe(2)-C(18)	2.0039(19)	C(7)-C(12)	1.396(3)
Fe(2)-C(13)	2.014(2)	C(7)-C(8)	1.410(3)
Fe(2)-C(19)	2.031(2)	C(8)-C(9)	1.395(3)
Fe(2)-C(17)	2.031(2)	C(13)-C(14)	1.445(3)
Fe(2)-C(14)	2.037(2)	C(13)-C(17)	1.449(3)
Fe(2)-C(22)	2.039(2)	C(14)-C(15)	1.435(3)
Fe(2)-C(20)	2.063(2)	C(22)-C(21)	1.425(3)
Fe(2)-C(16)	2.070(2)	C(22)-C(18)	1.443(3)
Fe(2)-C(21)	2.073(2)	C(21)-C(20)	1.415(4)
Fe(2)-C(15)	2.076(2)	C(19)-C(20)	1.429(3)
P(3)-C(13)	1.817(2)	C(19)-C(18)	1.443(3)
P(3)-C(7)	1.818(2)	C(17)-C(16)	1.424(4)
P(3)-C(1)	1.824(2)	C(15)-C(16)	1.424(4)
P(4)-C(18)	1.805(2)	C(27)-C(26)	1.395(4)
P(4)-C(23)	1.832(2)	C(27)-C(28)	1.399(3)
P(4)-C(29)	1.832(2)	C(23)-C(24)	1.402(3)
C(1)-C(6)	1.398(3)	C(23)-C(28)	1.407(3)
C(1)-C(2)	1.399(3)	C(24)-C(25)	1.402(3)
C(6)-C(5)	1.396(4)	C(26)-C(25)	1.392(4)

C(31)-C(32)	1.390(4)	C(13)-Fe(2)-C(17)	41.97(8)
C(31)-C(30)	1.392(3)	C(19)-Fe(2)-C(17)	175.14(9)
C(32)-C(33)	1.382(4)	C(18)-Fe(2)-C(14)	106.09(8)
C(33)-C(34)	1.399(3)	C(13)-Fe(2)-C(14)	41.78(9)
C(30)-C(29)	1.401(3)	C(19)-Fe(2)-C(14)	112.17(9)
C(29)-C(34)	1.399(3)	C(17)-Fe(2)-C(14)	69.61(9)
C(41)-C(42)	1.390(3)	C(18)-Fe(2)-C(22)	41.81(9)
C(41)-C(40)	1.505(3)	C(13)-Fe(2)-C(22)	106.40(9)
C(35)-C(36)	1.395(3)	C(19)-Fe(2)-C(22)	69.67(9)
C(35)-C(44)	1.513(4)	C(17)-Fe(2)-C(22)	112.75(9)
C(42)-C(43)	1.521(3)	C(14)-Fe(2)-C(22)	132.35(9)
C(36)-C(37)	1.515(3)	C(18)-Fe(2)-C(20)	69.52(8)
C(43)-C(44)	1.531(3)	C(13)-Fe(2)-C(20)	173.48(10)
C(40)-C(37)	1.544(3)	C(19)-Fe(2)-C(20)	40.86(9)
F(1)-B(1)	1.398(4)	C(17)-Fe(2)-C(20)	135.36(9)
B(1)-F(4)	1.390(3)	C(14)-Fe(2)-C(20)	144.70(10)
B(1)-F(3)	1.392(4)	C(22)-Fe(2)-C(20)	68.44(9)
B(1)-F(2)	1.405(3)	C(18)-Fe(2)-C(16)	173.16(10)
		C(13)-Fe(2)-C(16)	69.48(9)
C(35)-Rh(1)-C(36)	36.70(9)	C(19)-Fe(2)-C(16)	135.20(10)
C(35)-Rh(1)-C(41)	94.98(9)	C(17)-Fe(2)-C(16)	40.62(10)
C(36)-Rh(1)-C(41)	79.96(8)	C(14)-Fe(2)-C(16)	68.50(9)
C(35)-Rh(1)-C(42)	79.21(8)	C(22)-Fe(2)-C(16)	144.98(10)
C(36)-Rh(1)-C(42)	86.10(8)	C(20)-Fe(2)-C(16)	112.22(10)
C(41)-Rh(1)-C(42)	35.75(8)	C(18)-Fe(2)-C(21)	69.27(8)
C(35)-Rh(1)-P(4)	85.14(7)	C(13)-Fe(2)-C(21)	133.47(10)
C(36)-Rh(1)-P(4)	93.54(6)	C(19)-Fe(2)-C(21)	68.46(9)
C(41)-Rh(1)-P(4)	168.44(6)	C(17)-Fe(2)-C(21)	110.39(10)
C(42)-Rh(1)-P(4)	154.18(6)	C(14)-Fe(2)-C(21)	172.73(9)
C(35)-Rh(1)-P(3)	165.99(7)	C(22)-Fe(2)-C(21)	40.54(9)
C(36)-Rh(1)-P(3)	156.04(6)	C(20)-Fe(2)-C(21)	40.01(10)
C(41)-Rh(1)-P(3)	86.17(6)	C(16)-Fe(2)-C(21)	116.54(10)
C(42)-Rh(1)-P(3)	94.00(5)	C(18)-Fe(2)-C(15)	132.98(9)
P(4)-Rh(1)-P(3)	96.52(2)	C(13)-Fe(2)-C(15)	69.62(9)
C(18)-Fe(2)-C(13)	109.58(8)	C(19)-Fe(2)-C(15)	109.55(10)
C(18)-Fe(2)-C(19)	41.92(9)	C(17)-Fe(2)-C(15)	68.60(10)
C(13)-Fe(2)-C(19)	142.24(8)	C(14)-Fe(2)-C(15)	40.84(9)
C(18)-Fe(2)-C(17)	142.61(9)	C(22)-Fe(2)-C(15)	172.84(9)

C(20)-Fe(2)-C(15)	115.94(10)	C(15)-C(14)-Fe(2)	71.02(13)
C(16)-Fe(2)-C(15)	40.17(10)	C(13)-C(14)-Fe(2)	68.27(12)
C(21)-Fe(2)-C(15)	146.34(9)	C(21)-C(22)-C(18)	107.8(2)
C(13)-P(3)-C(7)	102.25(9)	C(21)-C(22)-Fe(2)	71.01(13)
C(13)-P(3)-C(1)	103.06(10)	C(18)-C(22)-Fe(2)	67.78(11)
C(7)-P(3)-C(1)	105.96(10)	C(20)-C(21)-C(22)	108.64(19)
C(13)-P(3)-Rh(1)	124.62(7)	C(20)-C(21)-Fe(2)	69.61(14)
C(7)-P(3)-Rh(1)	111.64(6)	C(22)-C(21)-Fe(2)	68.44(12)
C(1)-P(3)-Rh(1)	107.75(6)	C(20)-C(19)-C(18)	107.7(2)
C(18)-P(4)-C(23)	107.05(10)	C(20)-C(19)-Fe(2)	70.79(13)
C(18)-P(4)-C(29)	98.68(9)	C(18)-C(19)-Fe(2)	68.05(12)
C(23)-P(4)-C(29)	105.65(10)	C(16)-C(17)-C(13)	108.3(2)
C(18)-P(4)-Rh(1)	118.11(7)	C(16)-C(17)-Fe(2)	71.15(14)
C(23)-P(4)-Rh(1)	108.59(8)	C(13)-C(17)-Fe(2)	68.40(12)
C(29)-P(4)-Rh(1)	117.59(7)	C(21)-C(20)-C(19)	108.5(2)
C(6)-C(1)-C(2)	119.0(2)	C(21)-C(20)-Fe(2)	70.38(14)
C(6)-C(1)-P(3)	124.05(17)	C(19)-C(20)-Fe(2)	68.35(13)
C(2)-C(1)-P(3)	116.30(17)	C(16)-C(15)-C(14)	107.9(2)
C(5)-C(6)-C(1)	120.4(2)	C(16)-C(15)-Fe(2)	69.69(14)
C(3)-C(2)-C(1)	120.7(2)	C(14)-C(15)-Fe(2)	68.14(12)
C(3)-C(4)-C(5)	120.4(2)	C(15)-C(16)-C(17)	108.7(2)
C(4)-C(3)-C(2)	119.9(2)	C(15)-C(16)-Fe(2)	70.13(12)
C(6)-C(5)-C(4)	119.5(3)	C(17)-C(16)-Fe(2)	68.23(12)
C(11)-C(10)-C(9)	119.7(2)	C(22)-C(18)-C(19)	107.30(17)
C(10)-C(11)-C(12)	120.5(2)	C(22)-C(18)-P(4)	122.03(16)
C(12)-C(7)-C(8)	119.13(18)	C(19)-C(18)-P(4)	130.66(17)
C(12)-C(7)-P(3)	118.66(14)	C(22)-C(18)-Fe(2)	70.40(11)
C(8)-C(7)-P(3)	122.18(15)	C(19)-C(18)-Fe(2)	70.03(11)
C(9)-C(8)-C(7)	119.99(19)	P(4)-C(18)-Fe(2)	124.14(11)
C(8)-C(9)-C(10)	120.11(19)	C(26)-C(27)-C(28)	119.8(2)
C(11)-C(12)-C(7)	120.49(18)	C(24)-C(23)-C(28)	119.0(2)
C(14)-C(13)-C(17)	106.75(18)	C(24)-C(23)-P(4)	123.45(17)
C(14)-C(13)-P(3)	124.91(15)	C(28)-C(23)-P(4)	117.45(17)
C(17)-C(13)-P(3)	127.95(17)	C(27)-C(28)-C(23)	120.6(2)
C(14)-C(13)-Fe(2)	69.96(13)	C(23)-C(24)-C(25)	120.1(2)
C(17)-C(13)-Fe(2)	69.63(13)	C(25)-C(26)-C(27)	120.1(2)
P(3)-C(13)-Fe(2)	119.91(10)	C(32)-C(31)-C(30)	119.7(2)
C(15)-C(14)-C(13)	108.36(19)	C(33)-C(32)-C(31)	120.2(2)

C(32)-C(33)-C(34)	120.7(2)	C(35)-C(36)-Rh(1)	71.47(12)
C(31)-C(30)-C(29)	120.5(2)	C(37)-C(36)-Rh(1)	112.61(13)
C(34)-C(29)-C(30)	119.41(19)	C(42)-C(43)-C(44)	111.98(19)
C(34)-C(29)-P(4)	123.14(17)	C(41)-C(40)-C(37)	114.00(19)
C(30)-C(29)-P(4)	117.40(15)	C(35)-C(44)-C(43)	114.06(19)
C(42)-C(41)-C(40)	125.54(19)	C(36)-C(37)-C(40)	113.48(17)
C(42)-C(41)-Rh(1)	72.74(14)	C(29)-C(34)-C(33)	119.5(2)
C(40)-C(41)-Rh(1)	107.41(15)	C(26)-C(25)-C(24)	120.3(2)
C(36)-C(35)-C(44)	126.0(2)	F(4)-B(1)-F(3)	109.8(2)
C(36)-C(35)-Rh(1)	71.84(12)	F(4)-B(1)-F(1)	110.4(2)
C(44)-C(35)-Rh(1)	108.77(15)	F(3)-B(1)-F(1)	109.0(2)
C(41)-C(42)-C(43)	124.50(19)	F(4)-B(1)-F(2)	108.8(2)
C(41)-C(42)-Rh(1)	71.52(14)	F(3)-B(1)-F(2)	109.2(2)
C(43)-C(42)-Rh(1)	112.10(14)	F(1)-B(1)-F(2)	109.6(3)
C(35)-C(36)-C(37)	125.1(2)		

Table 3. Torsion angles [°] for **153**.

C(35)-Rh(1)-P(3)-C(13)	-83.1(3)
C(36)-Rh(1)-P(3)-C(13)	127.16(17)
C(41)-Rh(1)-P(3)-C(13)	-178.36(11)
C(42)-Rh(1)-P(3)-C(13)	-143.45(10)
P(4)-Rh(1)-P(3)-C(13)	12.92(9)
C(35)-Rh(1)-P(3)-C(7)	153.4(3)
C(36)-Rh(1)-P(3)-C(7)	3.70(17)
C(41)-Rh(1)-P(3)-C(7)	58.19(10)
C(42)-Rh(1)-P(3)-C(7)	93.10(10)
P(4)-Rh(1)-P(3)-C(7)	-110.53(8)
C(35)-Rh(1)-P(3)-C(1)	37.5(3)
C(36)-Rh(1)-P(3)-C(1)	-112.24(17)
C(41)-Rh(1)-P(3)-C(1)	-57.76(10)
C(42)-Rh(1)-P(3)-C(1)	-22.85(10)
P(4)-Rh(1)-P(3)-C(1)	133.53(8)
C(35)-Rh(1)-P(4)-C(18)	-160.98(11)
C(36)-Rh(1)-P(4)-C(18)	-125.22(10)
C(41)-Rh(1)-P(4)-C(18)	-69.9(3)
C(42)-Rh(1)-P(4)-C(18)	146.41(14)
P(3)-Rh(1)-P(4)-C(18)	33.00(8)
C(35)-Rh(1)-P(4)-C(23)	76.99(10)
C(36)-Rh(1)-P(4)-C(23)	112.75(9)

C(41)-Rh(1)-P(4)-C(23)	168.1(3)
C(42)-Rh(1)-P(4)-C(23)	24.38(14)
P(3)-Rh(1)-P(4)-C(23)	-89.03(7)
C(35)-Rh(1)-P(4)-C(29)	-42.80(11)
C(36)-Rh(1)-P(4)-C(29)	-7.04(10)
C(41)-Rh(1)-P(4)-C(29)	48.3(3)
C(42)-Rh(1)-P(4)-C(29)	-95.41(14)
P(3)-Rh(1)-P(4)-C(29)	151.18(8)
C(13)-P(3)-C(1)-C(6)	-124.35(18)
C(7)-P(3)-C(1)-C(6)	-17.3(2)
Rh(1)-P(3)-C(1)-C(6)	102.30(17)
C(13)-P(3)-C(1)-C(2)	64.64(17)
C(7)-P(3)-C(1)-C(2)	171.67(16)
Rh(1)-P(3)-C(1)-C(2)	-68.72(17)
C(2)-C(1)-C(6)-C(5)	-0.7(3)
P(3)-C(1)-C(6)-C(5)	-171.50(19)
C(6)-C(1)-C(2)-C(3)	0.4(3)
P(3)-C(1)-C(2)-C(3)	171.89(18)
C(5)-C(4)-C(3)-C(2)	-0.3(4)
C(1)-C(2)-C(3)-C(4)	0.1(4)
C(1)-C(6)-C(5)-C(4)	0.5(4)
C(3)-C(4)-C(5)-C(6)	0.0(4)
C(9)-C(10)-C(11)-C(12)	1.5(4)
C(13)-P(3)-C(7)-C(12)	-122.23(18)
C(1)-P(3)-C(7)-C(12)	130.16(18)
Rh(1)-P(3)-C(7)-C(12)	13.1(2)
C(13)-P(3)-C(7)-C(8)	56.0(2)
C(1)-P(3)-C(7)-C(8)	-51.6(2)
Rh(1)-P(3)-C(7)-C(8)	-168.63(16)
C(12)-C(7)-C(8)-C(9)	1.3(3)
P(3)-C(7)-C(8)-C(9)	-176.90(18)
C(7)-C(8)-C(9)-C(10)	-1.1(4)
C(11)-C(10)-C(9)-C(8)	-0.3(4)
C(10)-C(11)-C(12)-C(7)	-1.3(4)
C(8)-C(7)-C(12)-C(11)	-0.1(3)
P(3)-C(7)-C(12)-C(11)	178.20(18)
C(7)-P(3)-C(13)-C(14)	168.78(18)
C(1)-P(3)-C(13)-C(14)	-81.39(19)

Rh(1)-P(3)-C(13)-C(14)	41.3(2)
C(7)-P(3)-C(13)-C(17)	-3.1(2)
C(1)-P(3)-C(13)-C(17)	106.7(2)
Rh(1)-P(3)-C(13)-C(17)	-130.59(18)
C(7)-P(3)-C(13)-Fe(2)	83.41(13)
C(1)-P(3)-C(13)-Fe(2)	-166.76(11)
Rh(1)-P(3)-C(13)-Fe(2)	-44.06(15)
C(18)-Fe(2)-C(13)-C(14)	-92.49(12)
C(19)-Fe(2)-C(13)-C(14)	-58.64(18)
C(17)-Fe(2)-C(13)-C(14)	117.56(17)
C(22)-Fe(2)-C(13)-C(14)	-136.44(11)
C(20)-Fe(2)-C(13)-C(14)	-173.4(7)
C(16)-Fe(2)-C(13)-C(14)	80.30(13)
C(21)-Fe(2)-C(13)-C(14)	-172.09(12)
C(15)-Fe(2)-C(13)-C(14)	37.29(12)
C(18)-Fe(2)-C(13)-C(17)	149.95(13)
C(19)-Fe(2)-C(13)-C(17)	-176.20(15)
C(14)-Fe(2)-C(13)-C(17)	-117.56(17)
C(22)-Fe(2)-C(13)-C(17)	106.00(13)
C(20)-Fe(2)-C(13)-C(17)	69.0(7)
C(16)-Fe(2)-C(13)-C(17)	-37.26(14)
C(21)-Fe(2)-C(13)-C(17)	70.35(16)
C(15)-Fe(2)-C(13)-C(17)	-80.27(14)
C(18)-Fe(2)-C(13)-P(3)	27.04(15)
C(19)-Fe(2)-C(13)-P(3)	60.9(2)
C(17)-Fe(2)-C(13)-P(3)	-122.91(19)
C(14)-Fe(2)-C(13)-P(3)	119.53(16)
C(22)-Fe(2)-C(13)-P(3)	-16.91(14)
C(20)-Fe(2)-C(13)-P(3)	-53.9(7)
C(16)-Fe(2)-C(13)-P(3)	-160.17(15)
C(21)-Fe(2)-C(13)-P(3)	-52.56(16)
C(15)-Fe(2)-C(13)-P(3)	156.82(14)
C(17)-C(13)-C(14)-C(15)	0.3(2)
P(3)-C(13)-C(14)-C(15)	-173.03(16)
Fe(2)-C(13)-C(14)-C(15)	-59.92(15)
C(17)-C(13)-C(14)-Fe(2)	60.22(15)
P(3)-C(13)-C(14)-Fe(2)	-113.12(16)
C(18)-Fe(2)-C(14)-C(15)	-138.71(14)

C(13)-Fe(2)-C(14)-C(15)	119.72(17)
C(19)-Fe(2)-C(14)-C(15)	-94.66(14)
C(17)-Fe(2)-C(14)-C(15)	80.49(14)
C(22)-Fe(2)-C(14)-C(15)	-176.83(14)
C(20)-Fe(2)-C(14)-C(15)	-61.57(19)
C(16)-Fe(2)-C(14)-C(15)	36.87(14)
C(21)-Fe(2)-C(14)-C(15)	171.8(7)
C(18)-Fe(2)-C(14)-C(13)	101.57(12)
C(19)-Fe(2)-C(14)-C(13)	145.62(11)
C(17)-Fe(2)-C(14)-C(13)	-39.23(12)
C(22)-Fe(2)-C(14)-C(13)	63.45(15)
C(20)-Fe(2)-C(14)-C(13)	178.71(13)
C(16)-Fe(2)-C(14)-C(13)	-82.85(13)
C(21)-Fe(2)-C(14)-C(13)	52.1(8)
C(15)-Fe(2)-C(14)-C(13)	-119.72(17)
C(18)-Fe(2)-C(22)-C(21)	119.36(19)
C(13)-Fe(2)-C(22)-C(21)	-139.40(14)
C(19)-Fe(2)-C(22)-C(21)	80.26(15)
C(17)-Fe(2)-C(22)-C(21)	-95.21(15)
C(14)-Fe(2)-C(22)-C(21)	-177.81(14)
C(20)-Fe(2)-C(22)-C(21)	36.38(14)
C(16)-Fe(2)-C(22)-C(21)	-61.9(2)
C(15)-Fe(2)-C(22)-C(21)	165.3(7)
C(13)-Fe(2)-C(22)-C(18)	101.24(13)
C(19)-Fe(2)-C(22)-C(18)	-39.10(12)
C(17)-Fe(2)-C(22)-C(18)	145.43(13)
C(14)-Fe(2)-C(22)-C(18)	62.84(17)
C(20)-Fe(2)-C(22)-C(18)	-82.97(14)
C(16)-Fe(2)-C(22)-C(18)	178.72(16)
C(21)-Fe(2)-C(22)-C(18)	-119.36(19)
C(15)-Fe(2)-C(22)-C(18)	46.0(8)
C(18)-C(22)-C(21)-C(20)	-0.1(3)
Fe(2)-C(22)-C(21)-C(20)	-58.09(17)
C(18)-C(22)-C(21)-Fe(2)	57.95(14)
C(18)-Fe(2)-C(21)-C(20)	82.48(13)
C(13)-Fe(2)-C(21)-C(20)	-179.77(12)
C(19)-Fe(2)-C(21)-C(20)	37.39(12)
C(17)-Fe(2)-C(21)-C(20)	-137.56(13)

C(14)-Fe(2)-C(21)-C(20)	133.8(7)
C(22)-Fe(2)-C(21)-C(20)	120.89(19)
C(16)-Fe(2)-C(21)-C(20)	-93.57(15)
C(15)-Fe(2)-C(21)-C(20)	-55.8(2)
C(18)-Fe(2)-C(21)-C(22)	-38.41(13)
C(13)-Fe(2)-C(21)-C(22)	59.34(17)
C(19)-Fe(2)-C(21)-C(22)	-83.51(14)
C(17)-Fe(2)-C(21)-C(22)	101.55(14)
C(14)-Fe(2)-C(21)-C(22)	12.9(8)
C(20)-Fe(2)-C(21)-C(22)	-120.89(19)
C(16)-Fe(2)-C(21)-C(22)	145.53(14)
C(15)-Fe(2)-C(21)-C(22)	-176.74(16)
C(18)-Fe(2)-C(19)-C(20)	-119.17(19)
C(13)-Fe(2)-C(19)-C(20)	-170.93(14)
C(17)-Fe(2)-C(19)-C(20)	40.6(12)
C(14)-Fe(2)-C(19)-C(20)	151.17(14)
C(22)-Fe(2)-C(19)-C(20)	-80.16(14)
C(16)-Fe(2)-C(19)-C(20)	69.88(19)
C(21)-Fe(2)-C(19)-C(20)	-36.64(14)
C(15)-Fe(2)-C(19)-C(20)	107.41(15)
C(13)-Fe(2)-C(19)-C(18)	-51.76(19)
C(17)-Fe(2)-C(19)-C(18)	159.7(11)
C(14)-Fe(2)-C(19)-C(18)	-89.67(14)
C(22)-Fe(2)-C(19)-C(18)	39.00(12)
C(20)-Fe(2)-C(19)-C(18)	119.17(19)
C(16)-Fe(2)-C(19)-C(18)	-170.95(14)
C(21)-Fe(2)-C(19)-C(18)	82.53(14)
C(15)-Fe(2)-C(19)-C(18)	-133.43(13)
C(14)-C(13)-C(17)-C(16)	-0.2(2)
P(3)-C(13)-C(17)-C(16)	172.87(17)
Fe(2)-C(13)-C(17)-C(16)	60.23(17)
C(14)-C(13)-C(17)-Fe(2)	-60.43(14)
P(3)-C(13)-C(17)-Fe(2)	112.64(17)
C(18)-Fe(2)-C(17)-C(16)	-170.40(16)
C(13)-Fe(2)-C(17)-C(16)	-119.4(2)
C(19)-Fe(2)-C(17)-C(16)	32.0(12)
C(14)-Fe(2)-C(17)-C(16)	-80.36(16)
C(22)-Fe(2)-C(17)-C(16)	151.07(14)

C(20)-Fe(2)-C(17)-C(16)	69.26(19)
C(21)-Fe(2)-C(17)-C(16)	107.39(15)
C(15)-Fe(2)-C(17)-C(16)	-36.52(15)
C(18)-Fe(2)-C(17)-C(13)	-51.0(2)
C(19)-Fe(2)-C(17)-C(13)	151.4(11)
C(14)-Fe(2)-C(17)-C(13)	39.06(12)
C(22)-Fe(2)-C(17)-C(13)	-89.51(13)
C(20)-Fe(2)-C(17)-C(13)	-171.32(14)
C(16)-Fe(2)-C(17)-C(13)	119.4(2)
C(21)-Fe(2)-C(17)-C(13)	-133.19(13)
C(15)-Fe(2)-C(17)-C(13)	82.90(14)
C(22)-C(21)-C(20)-C(19)	-0.4(3)
Fe(2)-C(21)-C(20)-C(19)	-57.82(16)
C(22)-C(21)-C(20)-Fe(2)	57.38(16)
C(18)-C(19)-C(20)-C(21)	0.8(3)
Fe(2)-C(19)-C(20)-C(21)	59.07(17)
C(18)-C(19)-C(20)-Fe(2)	-58.22(15)
C(18)-Fe(2)-C(20)-C(21)	-81.79(13)
C(13)-Fe(2)-C(20)-C(21)	1.5(8)
C(19)-Fe(2)-C(20)-C(21)	-120.30(18)
C(17)-Fe(2)-C(20)-C(21)	64.20(17)
C(14)-Fe(2)-C(20)-C(21)	-170.91(14)
C(22)-Fe(2)-C(20)-C(21)	-36.85(12)
C(16)-Fe(2)-C(20)-C(21)	105.32(14)
C(15)-Fe(2)-C(20)-C(21)	149.33(12)
C(18)-Fe(2)-C(20)-C(19)	38.51(13)
C(13)-Fe(2)-C(20)-C(19)	121.8(7)
C(17)-Fe(2)-C(20)-C(19)	-175.50(14)
C(14)-Fe(2)-C(20)-C(19)	-50.6(2)
C(22)-Fe(2)-C(20)-C(19)	83.45(14)
C(16)-Fe(2)-C(20)-C(19)	-134.38(14)
C(21)-Fe(2)-C(20)-C(19)	120.30(18)
C(15)-Fe(2)-C(20)-C(19)	-90.36(14)
C(13)-C(14)-C(15)-C(16)	-0.3(3)
Fe(2)-C(14)-C(15)-C(16)	-58.51(17)
C(13)-C(14)-C(15)-Fe(2)	58.21(14)
C(18)-Fe(2)-C(15)-C(16)	-179.84(15)
C(13)-Fe(2)-C(15)-C(16)	81.97(15)

C(19)-Fe(2)-C(15)-C(16)	-138.30(15)
C(17)-Fe(2)-C(15)-C(16)	36.91(15)
C(14)-Fe(2)-C(15)-C(16)	120.1(2)
C(22)-Fe(2)-C(15)-C(16)	139.2(8)
C(20)-Fe(2)-C(15)-C(16)	-94.33(16)
C(21)-Fe(2)-C(15)-C(16)	-58.1(2)
C(18)-Fe(2)-C(15)-C(14)	60.08(18)
C(13)-Fe(2)-C(15)-C(14)	-38.11(13)
C(19)-Fe(2)-C(15)-C(14)	101.62(14)
C(17)-Fe(2)-C(15)-C(14)	-83.18(14)
C(22)-Fe(2)-C(15)-C(14)	19.1(8)
C(20)-Fe(2)-C(15)-C(14)	145.59(13)
C(16)-Fe(2)-C(15)-C(14)	-120.1(2)
C(21)-Fe(2)-C(15)-C(14)	-178.14(17)
C(14)-C(15)-C(16)-C(17)	0.2(3)
Fe(2)-C(15)-C(16)-C(17)	-57.38(17)
C(14)-C(15)-C(16)-Fe(2)	57.55(16)
C(13)-C(17)-C(16)-C(15)	0.0(3)
Fe(2)-C(17)-C(16)-C(15)	58.54(17)
C(13)-C(17)-C(16)-Fe(2)	-58.52(15)
C(18)-Fe(2)-C(16)-C(15)	1.0(9)
C(13)-Fe(2)-C(16)-C(15)	-82.36(15)
C(19)-Fe(2)-C(16)-C(15)	62.8(2)
C(17)-Fe(2)-C(16)-C(15)	-120.8(2)
C(14)-Fe(2)-C(16)-C(15)	-37.46(15)
C(22)-Fe(2)-C(16)-C(15)	-171.85(16)
C(20)-Fe(2)-C(16)-C(15)	104.41(16)
C(21)-Fe(2)-C(16)-C(15)	148.28(15)
C(18)-Fe(2)-C(16)-C(17)	121.8(8)
C(13)-Fe(2)-C(16)-C(17)	38.46(14)
C(19)-Fe(2)-C(16)-C(17)	-176.35(14)
C(14)-Fe(2)-C(16)-C(17)	83.35(15)
C(22)-Fe(2)-C(16)-C(17)	-51.0(2)
C(20)-Fe(2)-C(16)-C(17)	-134.78(14)
C(21)-Fe(2)-C(16)-C(17)	-90.90(16)
C(15)-Fe(2)-C(16)-C(17)	120.8(2)
C(21)-C(22)-C(18)-C(19)	0.7(2)
Fe(2)-C(22)-C(18)-C(19)	60.62(14)

C(21)-C(22)-C(18)-P(4)	-178.65(15)
Fe(2)-C(22)-C(18)-P(4)	-118.69(15)
C(21)-C(22)-C(18)-Fe(2)	-59.97(15)
C(20)-C(19)-C(18)-C(22)	-0.9(2)
Fe(2)-C(19)-C(18)-C(22)	-60.86(14)
C(20)-C(19)-C(18)-P(4)	178.31(17)
Fe(2)-C(19)-C(18)-P(4)	118.37(19)
C(20)-C(19)-C(18)-Fe(2)	59.94(15)
C(23)-P(4)-C(18)-C(22)	154.34(17)
C(29)-P(4)-C(18)-C(22)	-96.26(18)
Rh(1)-P(4)-C(18)-C(22)	31.53(19)
C(23)-P(4)-C(18)-C(19)	-24.8(2)
C(29)-P(4)-C(18)-C(19)	84.6(2)
Rh(1)-P(4)-C(18)-C(19)	-147.60(17)
C(23)-P(4)-C(18)-Fe(2)	67.42(16)
C(29)-P(4)-C(18)-Fe(2)	176.83(13)
Rh(1)-P(4)-C(18)-Fe(2)	-55.39(16)
C(13)-Fe(2)-C(18)-C(22)	-92.97(13)
C(19)-Fe(2)-C(18)-C(22)	117.73(18)
C(17)-Fe(2)-C(18)-C(22)	-59.51(19)
C(14)-Fe(2)-C(18)-C(22)	-136.82(13)
C(20)-Fe(2)-C(18)-C(22)	80.15(14)
C(16)-Fe(2)-C(18)-C(22)	-173.8(8)
C(21)-Fe(2)-C(18)-C(22)	37.28(14)
C(15)-Fe(2)-C(18)-C(22)	-172.97(14)
C(13)-Fe(2)-C(18)-C(19)	149.30(13)
C(17)-Fe(2)-C(18)-C(19)	-177.23(15)
C(14)-Fe(2)-C(18)-C(19)	105.46(13)
C(22)-Fe(2)-C(18)-C(19)	-117.73(18)
C(20)-Fe(2)-C(18)-C(19)	-37.57(13)
C(16)-Fe(2)-C(18)-C(19)	68.4(9)
C(21)-Fe(2)-C(18)-C(19)	-80.44(14)
C(15)-Fe(2)-C(18)-C(19)	69.31(17)
C(13)-Fe(2)-C(18)-P(4)	23.06(17)
C(19)-Fe(2)-C(18)-P(4)	-126.2(2)
C(17)-Fe(2)-C(18)-P(4)	56.5(2)
C(14)-Fe(2)-C(18)-P(4)	-20.79(17)
C(22)-Fe(2)-C(18)-P(4)	116.0(2)

C(20)-Fe(2)-C(18)-P(4)	-163.82(17)
C(16)-Fe(2)-C(18)-P(4)	-57.8(9)
C(21)-Fe(2)-C(18)-P(4)	153.31(17)
C(15)-Fe(2)-C(18)-P(4)	-56.9(2)
C(18)-P(4)-C(23)-C(24)	51.64(19)
C(29)-P(4)-C(23)-C(24)	-52.83(19)
Rh(1)-P(4)-C(23)-C(24)	-179.82(15)
C(18)-P(4)-C(23)-C(28)	-125.86(16)
C(29)-P(4)-C(23)-C(28)	129.67(16)
Rh(1)-P(4)-C(23)-C(28)	2.68(17)
C(26)-C(27)-C(28)-C(23)	-0.2(3)
C(24)-C(23)-C(28)-C(27)	-2.3(3)
P(4)-C(23)-C(28)-C(27)	175.30(17)
C(28)-C(23)-C(24)-C(25)	3.1(3)
P(4)-C(23)-C(24)-C(25)	-174.35(16)
C(28)-C(27)-C(26)-C(25)	1.9(4)
C(30)-C(31)-C(32)-C(33)	-0.6(4)
C(31)-C(32)-C(33)-C(34)	-0.3(4)
C(32)-C(31)-C(30)-C(29)	0.6(4)
C(31)-C(30)-C(29)-C(34)	0.3(3)
C(31)-C(30)-C(29)-P(4)	-177.25(19)
C(18)-P(4)-C(29)-C(34)	-124.73(19)
C(23)-P(4)-C(29)-C(34)	-14.2(2)
Rh(1)-P(4)-C(29)-C(34)	107.14(18)
C(18)-P(4)-C(29)-C(30)	52.69(19)
C(23)-P(4)-C(29)-C(30)	163.22(17)
Rh(1)-P(4)-C(29)-C(30)	-75.45(18)
C(35)-Rh(1)-C(41)-C(42)	-63.72(13)
C(36)-Rh(1)-C(41)-C(42)	-97.34(13)
P(4)-Rh(1)-C(41)-C(42)	-153.8(2)
P(3)-Rh(1)-C(41)-C(42)	102.27(11)
C(35)-Rh(1)-C(41)-C(40)	58.99(16)
C(36)-Rh(1)-C(41)-C(40)	25.37(14)
C(42)-Rh(1)-C(41)-C(40)	122.7(2)
P(4)-Rh(1)-C(41)-C(40)	-31.1(4)
P(3)-Rh(1)-C(41)-C(40)	-135.02(14)
C(41)-Rh(1)-C(35)-C(36)	-65.82(15)
C(42)-Rh(1)-C(35)-C(36)	-98.04(15)

P(4)-Rh(1)-C(35)-C(36)	102.58(14)
P(3)-Rh(1)-C(35)-C(36)	-160.0(2)
C(36)-Rh(1)-C(35)-C(44)	122.8(2)
C(41)-Rh(1)-C(35)-C(44)	56.98(18)
C(42)-Rh(1)-C(35)-C(44)	24.76(17)
P(4)-Rh(1)-C(35)-C(44)	-134.62(18)
P(3)-Rh(1)-C(35)-C(44)	-37.1(4)
C(40)-C(41)-C(42)-C(43)	5.2(4)
Rh(1)-C(41)-C(42)-C(43)	104.6(2)
C(40)-C(41)-C(42)-Rh(1)	-99.4(2)
C(35)-Rh(1)-C(42)-C(41)	114.58(14)
C(36)-Rh(1)-C(42)-C(41)	78.20(13)
P(4)-Rh(1)-C(42)-C(41)	168.28(11)
P(3)-Rh(1)-C(42)-C(41)	-77.78(12)
C(35)-Rh(1)-C(42)-C(43)	-6.01(16)
C(36)-Rh(1)-C(42)-C(43)	-42.38(16)
C(41)-Rh(1)-C(42)-C(43)	-120.6(2)
P(4)-Rh(1)-C(42)-C(43)	47.7(2)
P(3)-Rh(1)-C(42)-C(43)	161.63(15)
C(44)-C(35)-C(36)-C(37)	4.7(3)
Rh(1)-C(35)-C(36)-C(37)	105.06(19)
C(44)-C(35)-C(36)-Rh(1)	-100.4(2)
C(41)-Rh(1)-C(36)-C(35)	112.64(16)
C(42)-Rh(1)-C(36)-C(35)	77.14(15)
P(4)-Rh(1)-C(36)-C(35)	-76.99(14)
P(3)-Rh(1)-C(36)-C(35)	168.20(14)
C(35)-Rh(1)-C(36)-C(37)	-121.2(2)
C(41)-Rh(1)-C(36)-C(37)	-8.54(16)
C(42)-Rh(1)-C(36)-C(37)	-44.05(16)
P(4)-Rh(1)-C(36)-C(37)	161.82(15)
P(3)-Rh(1)-C(36)-C(37)	47.0(3)
C(41)-C(42)-C(43)-C(44)	-96.2(3)
Rh(1)-C(42)-C(43)-C(44)	-14.0(2)
C(42)-C(41)-C(40)-C(37)	41.8(3)
Rh(1)-C(41)-C(40)-C(37)	-39.1(2)
C(36)-C(35)-C(44)-C(43)	39.3(3)
Rh(1)-C(35)-C(44)-C(43)	-41.5(2)
C(42)-C(43)-C(44)-C(35)	37.2(3)

C(35)-C(36)-C(37)-C(40)	-92.7(2)
Rh(1)-C(36)-C(37)-C(40)	-10.0(2)
C(41)-C(40)-C(37)-C(36)	33.8(3)
C(30)-C(29)-C(34)-C(33)	-1.1(3)
P(4)-C(29)-C(34)-C(33)	176.22(18)
C(32)-C(33)-C(34)-C(29)	1.1(4)
C(27)-C(26)-C(25)-C(24)	-1.1(4)
C(23)-C(24)-C(25)-C(26)	-1.5(3)

Chapter 2

2

Introduction

Silver is a commonly used transition metal for catalysis in industry. The heterogeneous silver-catalyzed ethylene epoxidation has been used worldwide to produce ethylene oxide largely due to demand in the manufacture of ethylene glycol. Eastman further extended this process to epoxidize butadiene.[1] Similar processes such as direct oxidation of alcohols and oxidative activation of olefins and simple alkanes have attracted interest as well.[2] Other silver-based heterogeneous processes include NO_x reduction[3] and catalytic oxidation of CO to CO_2.[4] In the past several years, significant progresses have been made in the exploration of silver-based homogeneous catalysis, and it is reasonable to expect more silver-catalytic processes and applications in synthesis in the future.

1 Wilkinson, S. *Chem. Eng. News* **1999**, *77*, 27-28.

2 For oxidation or deydrogenation of alcohols, see: (a) Hoelderich, W. F.; *Catal. Today* **2000**, *62*, 115-130. (b) Jovanovic, N. N.; Marinova, C.; Stankovic, M.; Tuliev, G. *Heterog. Catal*. **1987**, *6*, 277-282. For oxidation and/or isomerization of olefins see: (c) La Ginestra, A.; Patrono, P.; Berardelli, M. L.; Galli, P.; Ferragina, C.; Massucci, M. A. *J. Catal*. **1987**, *103*, 346-356. (d) Cordi, E. M.; Falconer, J. L. *Appl. Catal. A* **1997**, *151*, 179-191. For activation of alkanes, see: (e) Bharadwaj, S. S.; Yokoyama, C.; Schmidt, L. D. *Appl. Catal*. *A* **1996**, *140*, 73-97. (f) Burk, M. J.; Crabtree, R. H. *J. Am. Chem. Soc*. **1987**, *109*, 8025-8032.

3 For a review see: Burch, R.; Breen, J. P.; Meunier, F. C. *Appl. Catal. B* **2002**, *39*, 283-303.

4 Gardener, S. D.; Hoflund, G. B.; Upchurch, B. T.; Schryer, D. R.; Kielin, E. J.; Schryer, J. *J. Catal*. **1991**, *129*, 114-120.

1. Silver-catalyzed transformations

In homogeneous catalyzed organic transformations, silver has mostly been used as either a Lewis acid or a co-catalyst. Nevertheless, recent studies have shown that silver species exhibited interesting catalytic activities functioning as a transition metal catalyst. In the following sections, these two behaviours will be disclosed.

1.1. Enantioselective allylations and aldol-type reactions

Enantioselective allylation of carbonyl compounds[5] and aldol synthesis[6] are important processes based on nucleophilic addition to carbonyl derivatives giving optically active homoallylic alcohols and β-hydroxy carbonyl compounds, respectively. These functional groups are often seen in natural products or biologically active molecules and therefore efficient and enantioselective methods to construct such functional groups are desired. Numerous chiral Lewis acid catalysts have been developed and applied for these processes.

Yamamoto and co-workers have shown that [Ag(OTf)binap] complex is an excellent chiral catalyst for the asymmetric allylation of aldehydes with allyltributyltin[7] as well as the asymmetric aldol reaction of tributyltin enlolates.[8] This catalyst can

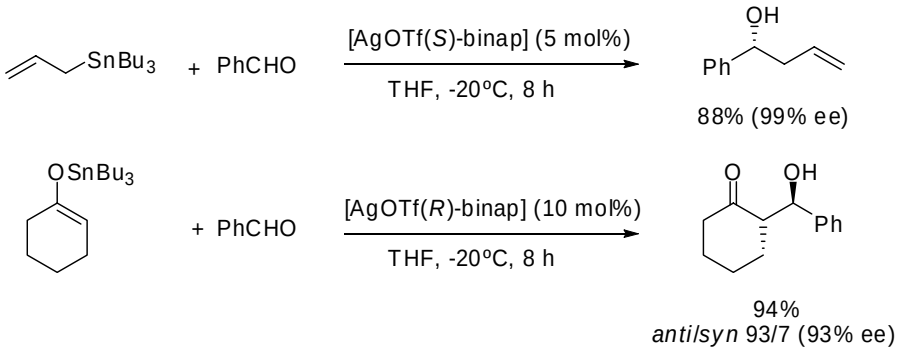
5 (a) Yamamoto, Y.; Asao, N. *Chem. Rev*. **1993**, *93*, 2207-2293. (b) Denmark, S. E.; Almostea, N. G. In *Modern Carbonyl Chemistry*: Otera, J., Ed.; Wiley-VCH: Weinhein, germany, **2000**, Chapter 10, p 299. (c) *Lewis Acids in Organic Synthesis*; Yamamoto, H., E.; Wiley-VCH: Weinheim, Germany, **2000**; Vols. 1 and 2.

6 Review for catalytic asymmetric aldol reactions: (a) Gennanri, C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C.H., Eds.; Pergamon Press: Oxford, UK, **1991**; Vol. 2, p 629. (b) Carreira, E. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, Germany, **1999**, Vol. 3, p 997. (c) Carreira, E. M. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wieley-VCH: Weinheim, Germany, **2000**; Chapter 8, p 227.

7 (a) Yanagisawa, A.; Nakashima, H.; Inhiba, A.; Yamamoto, H. *J. Am. Chem. Soc*. **1996**, *118*, 4723-4724.

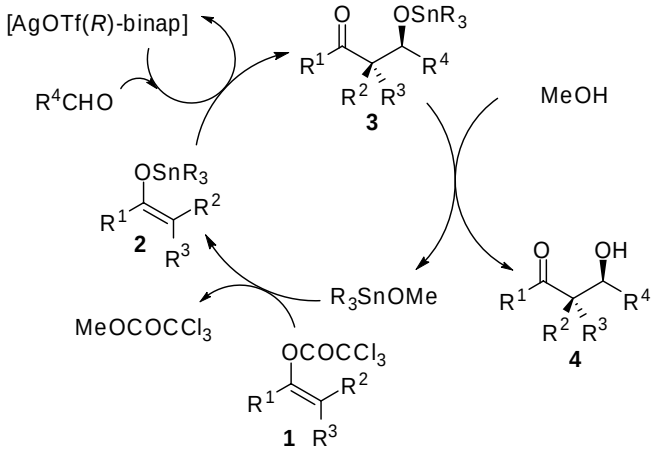
8 (a) Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc*. **1997**, *119*, 9319-9320. (b) Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc*. **1997**, *119*, 9319-9320. (c) Yanagisawa, A.; Matsumoto, Y.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc*. **1999**, *121*, 892-893. (c) Yanagisawa, A.; Matsumoto, Y.; Asakawa, K.; Yamamoto, H. *Tetrahedron* **2002**, *58*, 8331-8339.

provide the corresponding optically active products with high diastereo- and enantioselectivities (Scheme 1).



Scheme 1

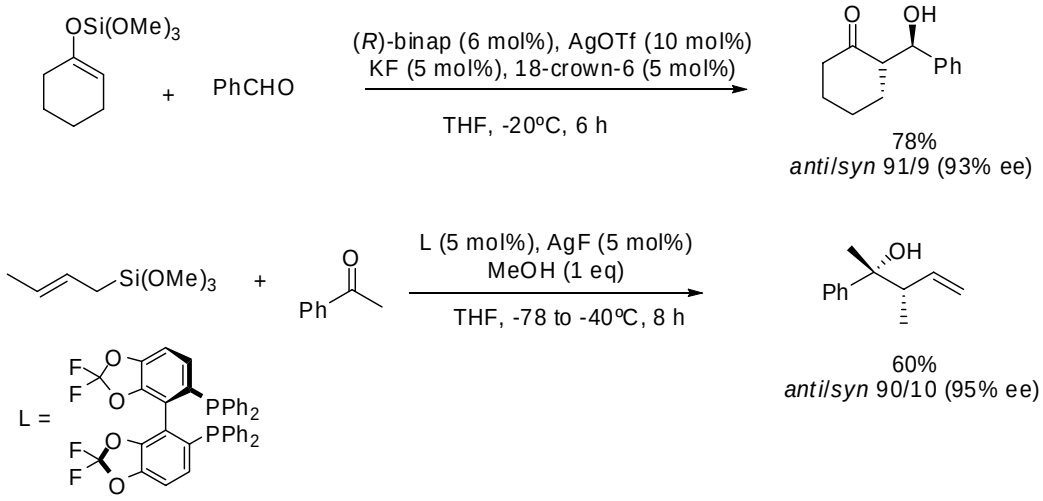
The reactions proceeded smoothly at low temperatures. In the case of the asymmetric allylations, not only aromatics but also α,β-unsaturated aldehydes could be used affording exclusively the 1,2-addition reaction products. The aldol reaction had a diastereoselecitvity markedly different from that of ordinary Mukaiyama type aldol reaction furnishing the *anti* aldol adduct preferentially. To avoid the disadvantage of requiring stoichiometric amounts of the toxic trialkyltin compounds, an aldol condensation using catalytic amount of tin enolate was investigated.[8c,d] In this case, the tin enolate **2** was generated from tributyltin metoxide and a trichloroactoxy enol (**1**) (Scheme 2). In the presence of MeOH the resulting tin alkoxide **3** was protonated yielding the initial tin methoxide (the protonation of the aldol adduct **3** was found to be faster than the protonation of the *in situ* generated tin enolate **2**).



Scheme 2

Allyltrimetoxysilanes and trimetoxysilyl enol ethers, which are less reactive than the tin counterparts, required and additional activation by fluoride atoms to give the

products. This was achieved by addition of catalytic amount of KF and 18-crown-6-ether or by changing AgOTf to AgF in the presence of MeOH to favour the solubility of the salt (Scheme 3).[9]



Scheme 3

Remarkably, in the allylation reaction, γ and *anti*-selectivities were observed for the reaction with crotyltrimethoxysilanes, irrespective of the configuration at the double bond. On the contrary, the stereoselectivity of the aldol reaction depended on the geometry of the trimethoxysilyl enol ether. Thus, (*E*)-trimethoxysilyl enol ether gave *anti*-products, whereas (*Z*)-trimethoxysilyl enol ether afforded the *syn*-adduct with high selectivity. Interestingly, when the reaction was accomplished in the absence of the silver complex, the opposite *syn*-selectivity was obtained. These results suggested that cyclic transition state structures (A and B, Figure 1) are probable models of the reaction mechanism.

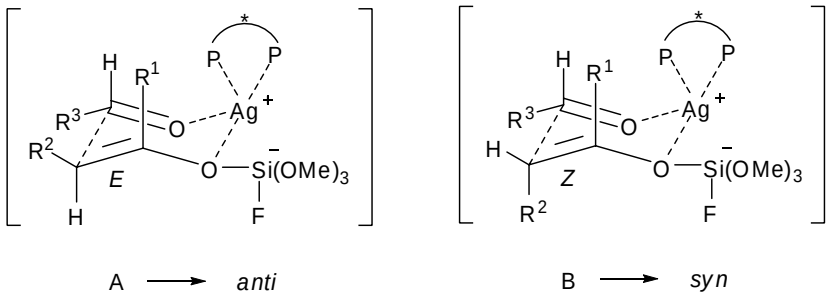


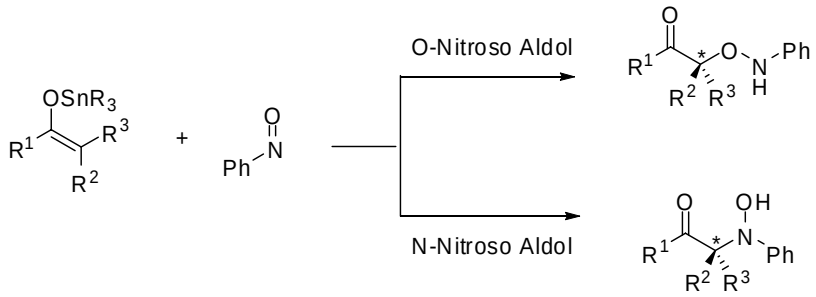
Figure 1

In these assemblies, the role of the Ag(I)-binap complex is to coordinate as a chiral Lewis acid to both the aldehydes and the silyl enol ether, to form a six-membered

9 (a) Wadamoto; M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem*. **2003**, *68*, 5593-5601. (b) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc*. **2005**, *127*, 14556-14557.

cyclic structure, in which the fluoride ion activates the silyl enol ether. For the allylation reaction, it was also proposed that silver acts as a chiral Lewis acid instead of acting as an allylsilver reagent. This was based on the fact that when equimolar amounts of the [Ag(OTf)(*S*)-binap] complex and allyltributyltin were mixed no reaction took place until the addition of an aldehyde.

Enantioselective nitroso-aldol reactions from tin enolates and nitrosobenzene were also found to be catalyzed by chiral silver(I) complexes (Scheme 4).[10]



Scheme 4

The *O*-/*N*- regioselectivity of the aldol reaction depended on the used silver(I)-binap complex. In an effort to investigate the coordination of binap with silver, low-temperature NMR studies were performed. It was found that by mixing 1 equiv of AgOTf with (*R*)-binap, three different complexes were formed:

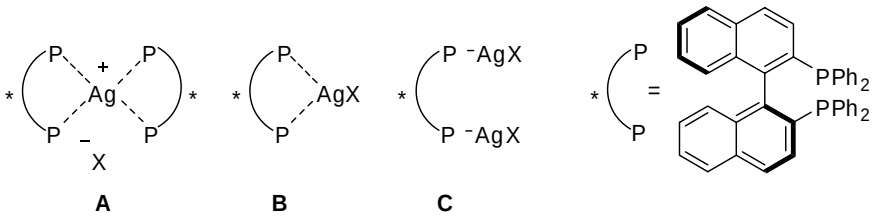


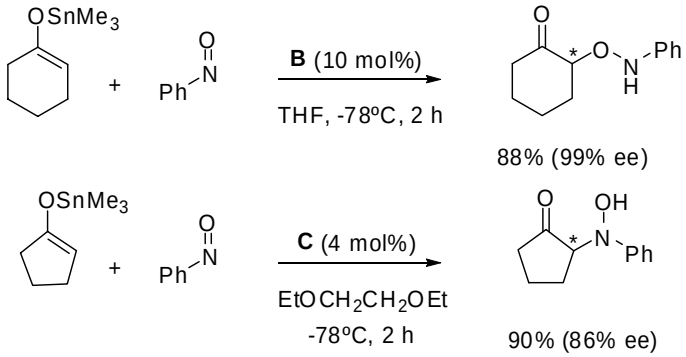
Figure 2

The isolation of each metal species could be achieved by adjusting the metal-to-ligand ratio. Using isolated complexes, it was observed that complex **B** catalyzes the *O*-selective nitroso aldol process, while complex **C** led to *N*-selectivity. In both processes, yields and enantioselectivities were high (Scheme 5).

The use of [AgF(*R*)-binap] as chiral catalyst in MeOH also allowed the synthesis of various nonracemic ketones with enantioselectivities of up to 99% *ee* by chiral protonation of silyl enolates. Again, it was postulated that the role of the silver complex was to act as a chiral Lewis acid.[11]

10 (a) Momiyama, N.; Yamamoto, H. *J. Am. Chem.Soc*. **2003**, *125*, 6038-6039. (b) Momiyama, N.; Yamamoto, H. *J. Am. Chem Soc*. **2004**, *126*, 5360-5361.

11 Yanagisawa, A.; Rouge, T.; Arai, T. *Angew. Chem. Int. Ed*. **2005**, *44*, 1546-1548.



Scheme 5

1.2. Nucleophilic addition reactions

Due to the well-established ability of silver(I) salts to form strong π-complexes,[12,13] silver(I) has been used to activate allenes, alkenes and alkynes to promote the intramolecular addition of nitrogen and oxygen nucleophiles for the synthesis of heterocycles compounds. Although scarcer, there also some examples of intermolecular nucleophilic addition to alkenes and alkynes catalyzed by silver(I).

1.2.1. Intramolecular nucleophilic addition reactions

Allenic moieties were successfully used for the synthesis of nitrogen as well as oxygen-containing heterocycles. Initial work came from the group of Gallagher, which used allenic amines for the synthesis of pyrrolidines in the presence of substoichiometric amounts of AgOTf.[14] To induce asymmetry in the cyclization process a sulfoxide group was introduced (Scheme 6). A similar methodology was applied for the synthesis of nitrone cycloadducts.[15] In the group of Marshall, silver(I) catalyzed

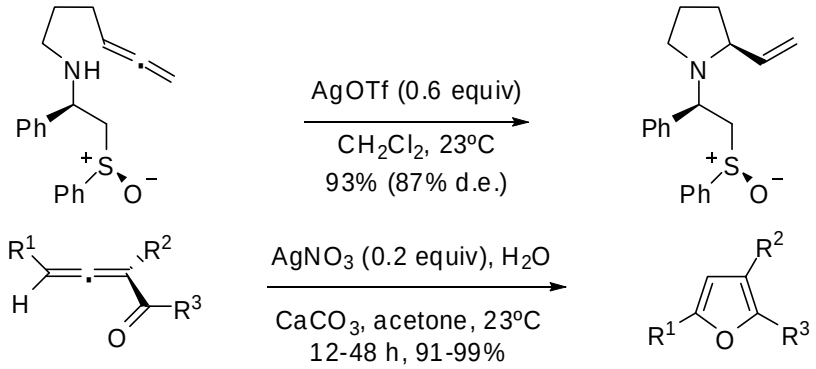
12 For reviews encompassing Ag(I)-alkene complexes, see: (a) Bennett, M. A. *Chem. Rev*. **1962**, *62*, 611-652. (b) Herberhold, M. In *Metal-π-Complexes*; Elsevier: Amsterdam, 1972; Vol. 2, pp 232-256.

13 For selected examples of Ag(I)-alkyne complexes characterized by single-crystal X-ray diffraction analysis, see: (a) Ferrara, J. D.; Djebli, A.; Tessier-Youngs, C.; Youngs, W. *J. Am. Chem. Soc*. **1988**, *110*, 647-649. (b) Nishinaga, T.; Kawamura, T.; Komatsu, K. *Chem. Commun*. **1998**, 2263-2264. (c) Chi, K.-M.; Lin, C.-T.; Peng, S.-M.; Lee, G.-H. *Organometallics* **1996**, *15*, 2662-2663.

14 (a) David, N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *Chem. Commun*. **1989**, 1073-1075. (b) Davies, I. W.; Gallagher, T.; Lamont, R. B.; Scopes, D. I. C. *Chem. Commun.* **1992**, 335-337.

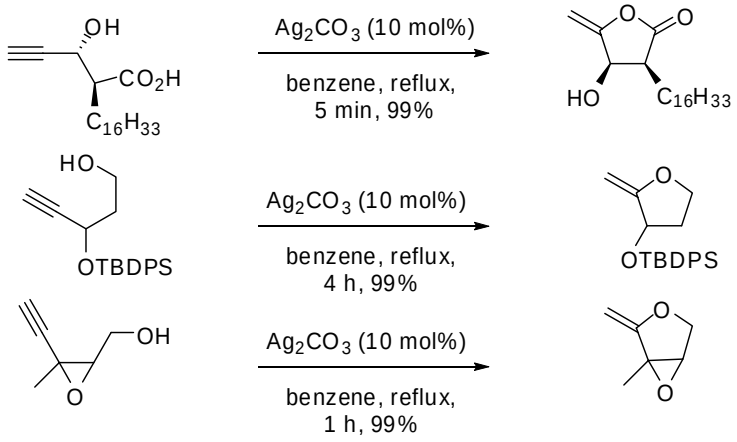
15 Lathbury, D. C.; Shaw, R. W.; Bates, P. A.; Hursthouse, M. B.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1*. **1989**, 2415-2424.

isomerization of allenyl ketones and aldehydes was used for the preparation of substituted furans in good yields (Scheme 6).[16] If alcohols, instead of ketones or aldehydes, are employed, the corresponding 2,5-dihydrofurans are obtained.



Scheme 6

Acetylenic alcohols and acids could be efficiently cyclized by a catalytic amount of silver carbonate in refluxing benzene.[17] The cyclization proved to be regioselective and the exocyclic α-methylene heterocycles resulting from an *exo-dig* ring closure were always isolated as the only product. The presence of oxygen substituents at the propargylic position accelerates the ring closure of both acetylenic alcohols and acids even when bulky substituents were present (Scheme 7).



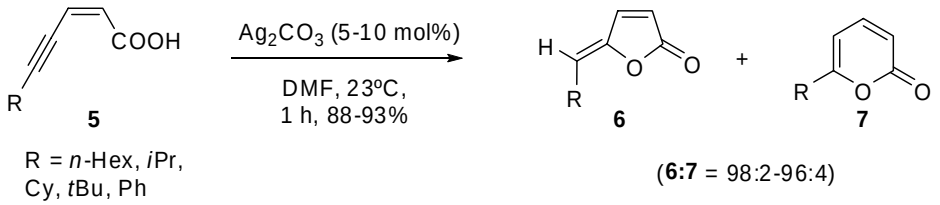
Scheme 7

Lactonization of (*Z*)-5-alkyl-2-en-4-yonic acids (**5**) by Ag_2CO_3 provides selective synthesis of (*Z*)-5-alkylidenefuran-2(5*H*)-ones (**6**) along with minor amounts

16 (a) Marshall, J. A.; Wang, X.-J. *J. Org. Chem*. **1991**, *56*, 960-969. (b) Bartley, G. S.; Marshall, J. A. *J. Org. Chem*. **1994**, *59*, 7169-7171. (c) Pinney, K. G.; Marshall, J. A. *J. Org. Chem*. **1993**, *58*, 7180-7184.

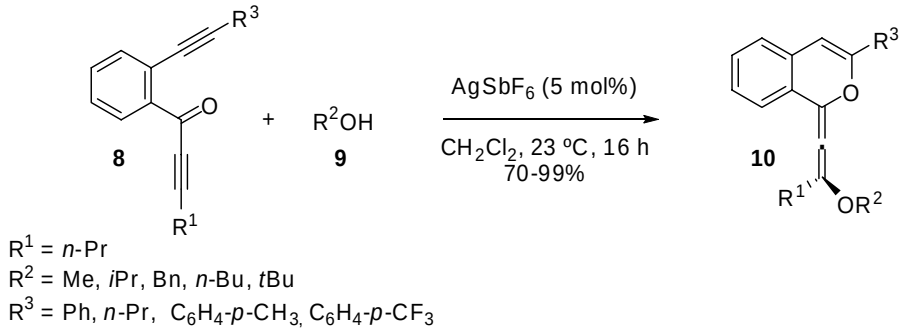
17 (a) Pale, P.; Chuche, J. *Tetrahedron Lett*. **1987**, *28*, 6447-6448. (b) Dalla, V.; Pale, P. *New. J. Chem*. **1999**, *23*, 803-805. (c) Chuche, J.; Pale, P. *Eur. J. Org. Chem*. **2000**, 1019-1025.

of 6-alkyl-2*H*-pyran-2-ones (**7**) in high yields. The regioselectivity observed in this cyclization was complementary to the one obtained when $ZnBr_2$ was employed as catalyst.[18]



Scheme 8

Stereoselective access to 1-allenyl chromenes **10** from alkynones **8** was possible by a silver-catalyzed cascade cyclization reaction. The reaction proceeded under very mild conditions and the obtained yields were good, although sterically hindered alcohols led to lower yields of the annulation products. Terminal or TMS-substituted alkynes (R^1 = H, TMS) did not give the corresponding desired products (Scheme 9).[19]



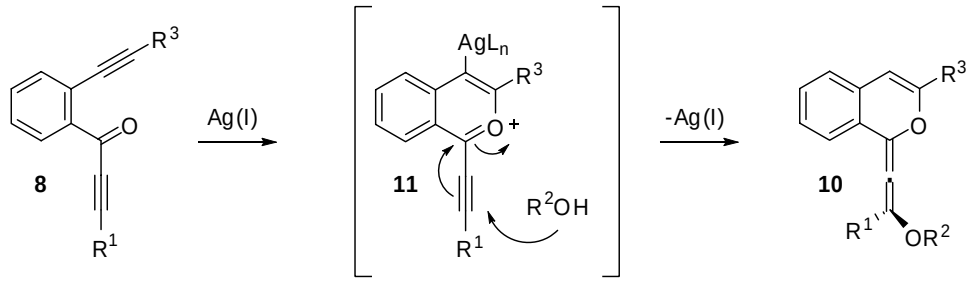
Scheme 9

The proposed reaction mechanism for this silver(I) catalyzed annulation is depicted in Scheme 10. Nucleophilic attack of the carbonyl oxygen to the silver coordinated alkyne would form benzopyrylidium cation **11**, which would undergo subsequent trapping with alcohols. Finally, protonation and regeneration of the Ag(I) catalyst would produce the annulation product **10**. The formation of the benzopyrylium cation **11** was supported by NMR experiments.[20]

18 Anastasia, L.; Xu, C.; Negishi, E.-I. *Tetrahedron Lett*. **2002**, *43*, 5673-5676.

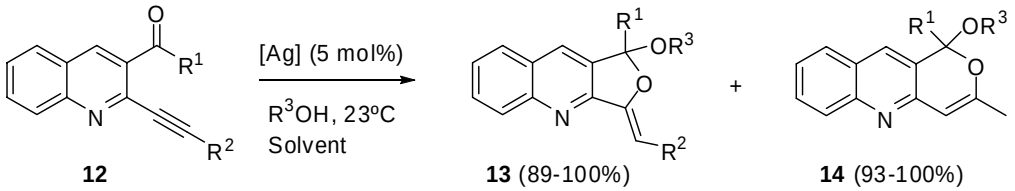
19 Patil, N. T.; Pahadi, N. K.; Yamamoto, Y. *J. Org. Chem*. **2005**, *70*, 10096-10098.

20 Benzopyrilium intermediates of type **11** are also involved in cycloisomerization-homodimerization processes of alkynyl benzaldehydes catalyzed by silver, see: Beeler, A. B.; Su, S.; Singleton, C. A.; Porco, J. A. *J. Am. Chem. Soc*. **2007**, *129*, 1413-1419



Scheme 10

A related process has recently been described in which furoquinolines **13** and pyranoquinolines **14** are obtained via an acetalization/cycloisomerization tandem reaction.[21] The regiochemistry of the reaction depended on the type of silver catalyst which was used. Silver salts which are known to form π-complexes with alkynes ($AgSbF_6$, $AgPF_6$, AgOTf, and $AgNO_3$), allowed an efficient transformation of quinoline derivatives **12** to the 6-*endo-dig* products **14**. Silver salts like Ag_2CO_3, Ag_2O and AgO, characterized for their oxidizing properties, gave the reverse selectivity affording the 5-*exo-dig* products **13**. It was proposed that compounds of type **13** came from an initial activation of the oxygen atom of the aldehyde function by coordination of the silver salts, whereas products of type **14** originated from an initial activation of the alkyne.

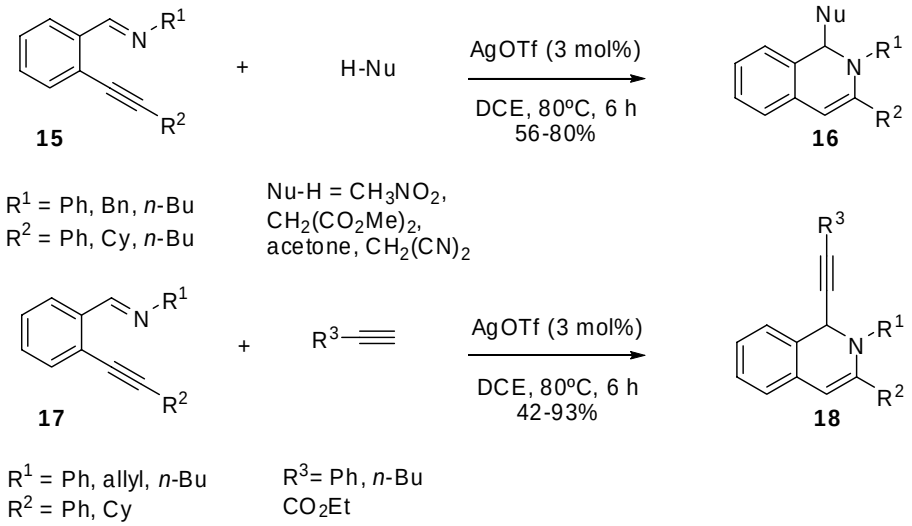


Scheme 11

Functionalized 1,2-dihydroisoquinolines **16** could be prepared by a silver-catalyzed direct Mannich reaction of pronucleophiles to non-activated imines **15** (Scheme 12).[22] Interestingly, not only activated methylenes but also simple terminal alkynes could be employed as pronucleophiles. The presence of the alkyne was found to be necessary for the addition of the pronucleophile to the imine, since in absence of alkynyl groups the imine substrate was recovered unchanged. This direct pronucleophile addition could be also applied to pyridine derivatives for the synthesis of naphtypyridine derivatives.

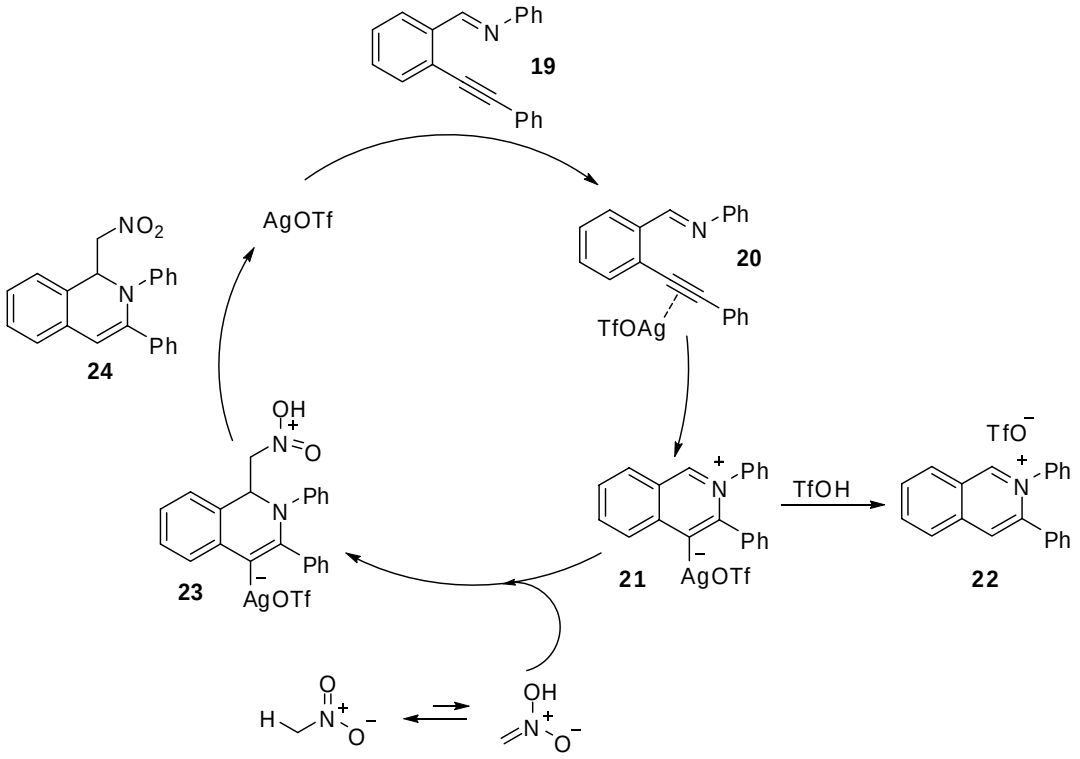
21 Godet, T.; Vaxelaire, C.; Michel, C.; Milet, A.; Belmont, P. *Chem. Eur. J.* **2007**, *13*, 5632-5641.

22 Asao, N.; Yudha, S.; Nogami, T.; Yamamoto, Y. *Angew. Chem. Int. Ed*. **2005**, *44*, 5526-5528.



Scheme 12

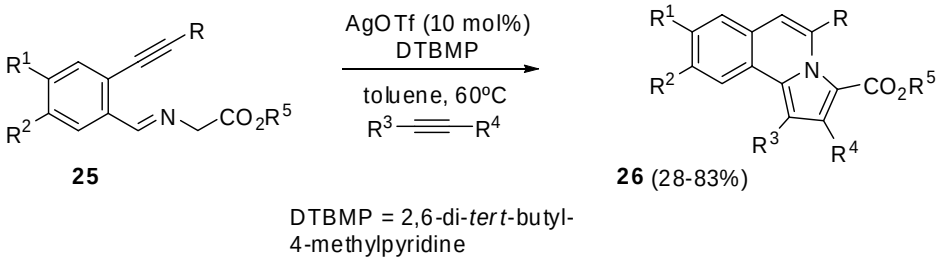
The proposed reaction mechanism starts with the coordination of the silver salt to the triple bond (**20**) (Scheme 13). Subsequent attack of the nitrogen atom at the electron-deficient triple bond would lead to the isoquinolinium intermediate **21**. Thereafter, the addition of aci-nitromethane would give the product **24** via alkenylsilver intermediate **23**.



Scheme 13

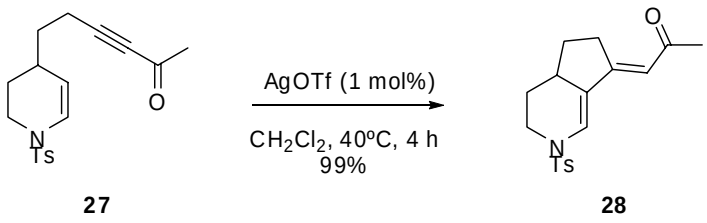
This mechanistic proposal was confirmed by crystallization of isoquinolinium salt **22** after treatment of **19** with AgOTf in the absence of any pronucleophile, followed

by addition of TfOH.[22] Similarly, isoquinolinium intermediates of type **21** formed from alkynyl imines **25** with and electron-withdrawing group at the imine moiety (Scheme 14), undergo [3+2] dipolar cycloadditions in the presence of AgOTf.[23] In this process pyrrolo-isoquinolines **26** are obtained with high regioselectivity.



Scheme 14

Enesulfonamides cyclize onto electron-deficient alkynes with silver catalysts to afford functionalized azahydrindan ring systems (**28**). Yields for this process range from 47 to 99% and the final products obtained can be reacted further using the Diels-Alder reaction.[24]



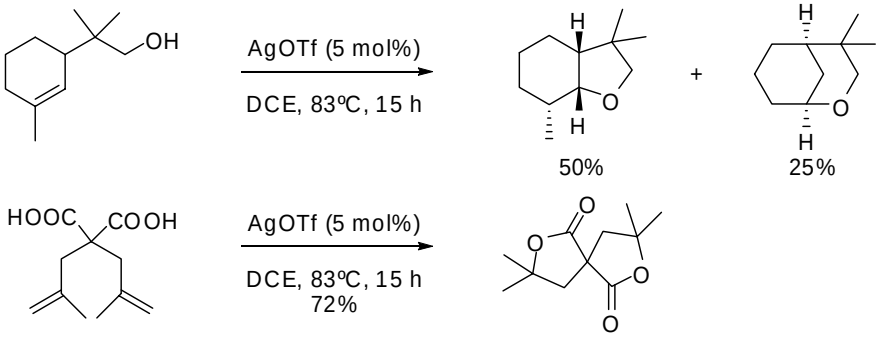
Scheme 15

Silver(I) triflate also catalyzes intramolecular additions of hydroxyl or carboxyl groups to olefins, a reaction that provides a simple access to cyclic ethers and lactones.[25] The reaction is general for alkenes bearing various substitutions at the α, β, and γ-carbon atoms and tolerates different functional groups. It is also applicable to the synthesis of fused- and spirobicyclic ethers in good yields (Scheme 16). The proposed mechanism for the hydroxyalkoxylation involves the activation of the double bond by a silver(I) ion which is then attacked by the oxygen-nucleophile on the opposite face.

23 Su, S.; Porco, J. A. *J. Am. Chem. Soc*. **2007**, *129*, 7744-7745.

24 Tyler, J. H.; Dake, G. R. *Org. Lett*. **2004**, *6*, 5023-5026.

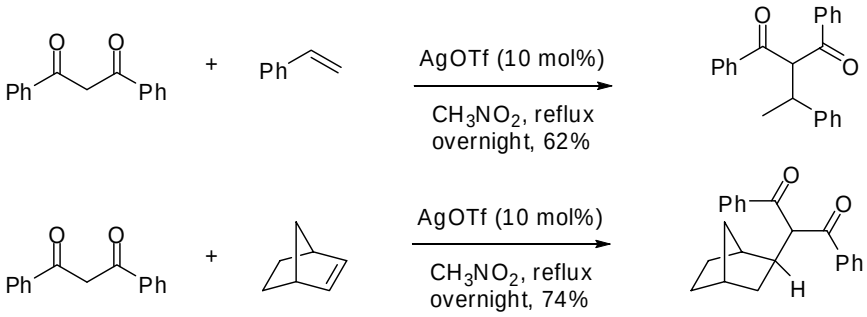
25 Yang, C.-G.; Reich, N. W.; Shi, Z.; He, C. *Org. Lett*. **2005**, *7*, 4553-4556.



Scheme 16

1.2.1. Intermolecular nucleophilic addition reactions

In the examples described before, silver(I) has been only used for the formation of C-O and C-N bonds. Although scarce, some examples where silver(I) is used for the formation of new C-C bonds have been reported. 1,3-Diketones are able to undergo additions to alkenes in the presence of AgOTf.[26] Compared with the same reaction catalyzed by gold,[27] the silver catalysis was more sensitive to steric effects and needed higher temperature to exhibit a good catalytic activity. The anion of the silver salt proved to be very important for the reaction; only triflate showed good catalytic activity. The intramolecular version of this reaction afforded the corresponding six-membered-ring products effectively. However, no C-alkylation products were observed when nonconjugated alkenes were employed for the intramolecular version.[26]



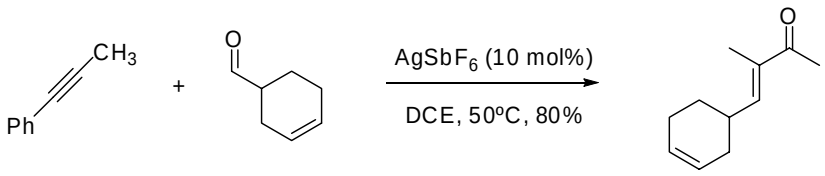
Scheme 17

Upon exposure to $AgSbF_6$, alkynes and aldehydes undergo intra- and intermolecular alkyne-carbonyl coupling to provide trisubstituted enones. The reaction

26 Yao, X.; Li, C.-J. *J. Org. Chem*. **2005**, *70*, 5752-5755.

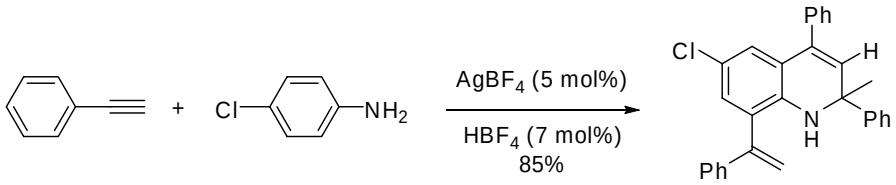
27 (a) Yao, X. Q.; Li, C.-J. *J. Am. Chem. Soc*. **2004**, *126*, 6884-6885. (b) Nguyen, R.-V.; Yao, X. Q.; Bohle, D. S.; Li, C.-J. *Org. Lett*. **2005**, *7*, 673-675.

can be considered as a formal alkyne-carbonyl metathesis.[28] Notably, high regio- and stereocontrol were observed.



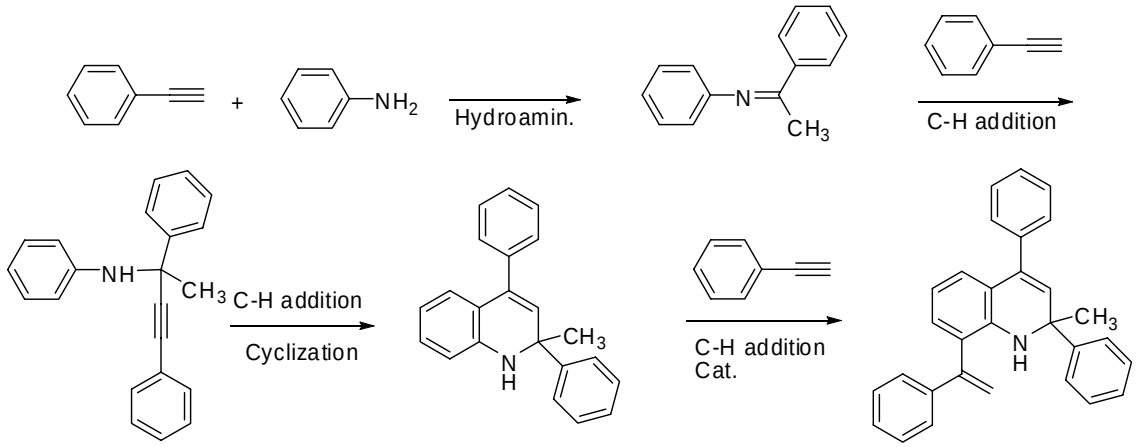
Scheme 18

By using silver salts, molecules of high complexity have been prepared from simple anilines and alkynes. Polysubstituted 1,2-dihydroquinoline derivatives **29** were generated in a one-pot domino process with high regioselectivity (Scheme 19).[29] Hydroamination, alkyne addition, intramolecular hydroarylation, and hydroarylation of a third molecule of alkyne could be accomplished in a one-pot process with 100% atom economy (Scheme 20). The reaction proceeded under solvent-free conditions. Interestingly, the Au-catalyzed reaction under the same reaction conditions afforded only the hydroamination products.



29

Scheme 19

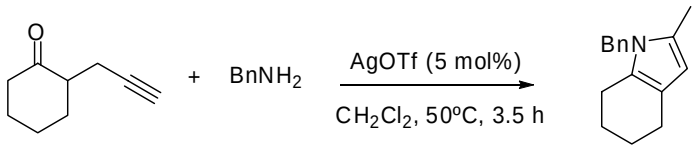


Scheme 20

28 Rhee, J. U.; Krische, M. J. *Org. Lett*. **2005**, *7*, 2493-2495.

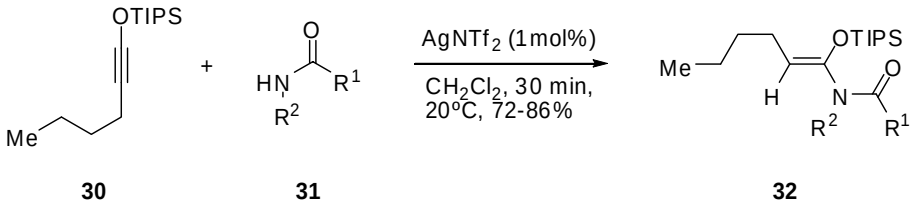
29 Luo, Y.; Li, Z.; Li, C.-J. *Org. Lett*. **2005**, *13*, 2675-2678.

Functionalized pyrroles could be efficiently synthesized by reaction between imines (formed *in situ*) and alkynes (Scheme 21).[30] The yields for these reactions were generally good, except when sterically demanding amines such as aniline, cyclohexylamine or *tert*-butyl amine were used. Although the same reaction was catalyzed by gold(I), the reactions catalyzed by the silver salts proceeded faster. Pyrroles have also been prepared in a one-pot synthesis via the silver-mediated reaction of secondary vinylogous amides or carbamates with propargyl bromide.[31]



Scheme 21

Hydroamination of electron-rich alkynes such as siloxy alkynes (**30**), with either secondary amides or carbamates (**31**) has also been performed with silver salts.[32] The process is *syn*-selective and represents an efficient method for the synthesis of a range of synthetically useful silyl ketene aminals (**32**). Notably, the catalyst loading could be lowered to 1 mol% (Scheme 22). Mechanistic studies demonstrated that the reaction proceeded by a fast and reversible silver-alkyne complexation, followed by a rate-determining C-N bond-forming step.



Scheme 22

Silver trifluoromethanesulfonimide ($AgNTf_2$) also promotes the [2+2] cycloaddition of siloxy alkynes with unsaturated ketones, ester, and nitriles.[33] This transformation presumably takes place via a silver-based activation of the siloxy alkyne toward subsequent 1,4-addition and a stepwise cycloaddition. The stepwise cycloaddition mechanism is consistent with the fact that the same *trans*-substituted

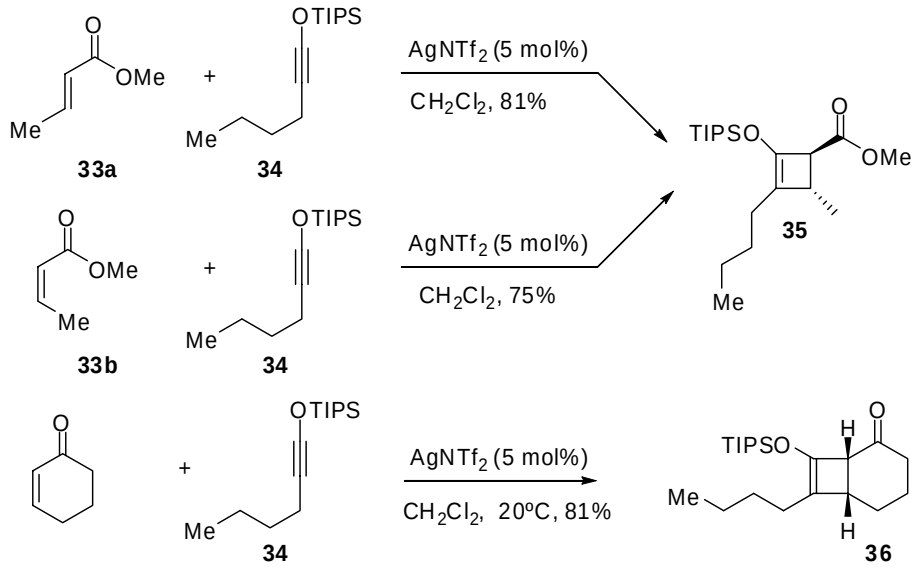
30 Harrison, T. J.; Kozak, J. A.; Corbella-Pané, M.; Dake, G. R. *J. Org. Chem*. **2006**, *71*, 4525-4529.

31 Robiannson, R. S.; Dovey, M. C.; Gravestock, D. *Tetrahedron Lett*. **2004**, *45*, 6787-6789.

32 Sun, J.; Kozmin, S. A. *Angew. Chem. Int. Ed*. **2006**, *45*, 4991-4993.

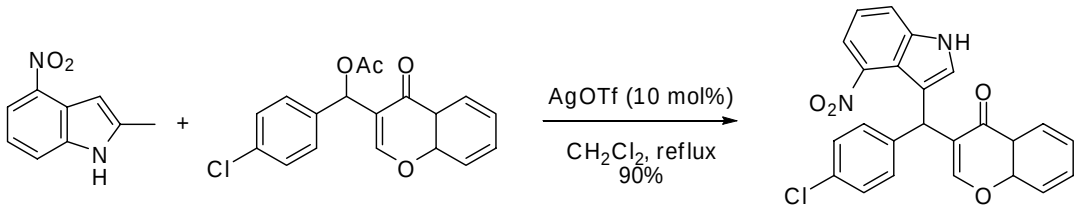
33 Sweis, R. F.; Schramm, M. P.; Kozmin, S. A. *J. Am. Chem. Soc*. **2004**, *126*, 7442-7443.

siloxy cyclobutene (**35**) was obtained regardless of the *E*- or *Z*- configuration of the α,β-unsaturated ester (**33a**, **33b**) employed (Scheme 23). By this method, bicyclic silyl enol ether **36** was obtained from cyclohexenone and siloxy alkyne **34**. This process provides an efficient method for the assembly of highly functionalized siloxy cyclobutenes.



Scheme 23

Very recently it has been shown that silver is not only able to promote nucleophilic additions to π-bonds, but that can also promote nucleophilic substitution with indoles.[34] The reaction is α-regioselective and leads to products in good to excellent yields with indoles bearing either electron-withdrawing or electron-donating groups.

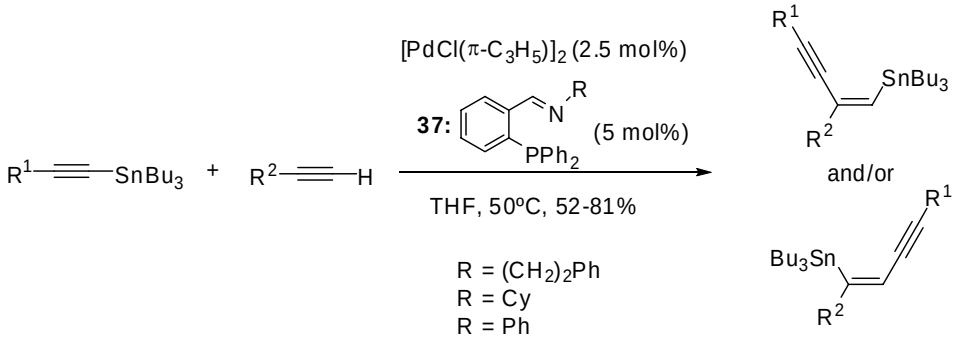


Scheme 24

34 Shafiq, Z.; Liu, L.; Liu, Z.; Wang, D.; Chen, Y.-J. *Org. Lett*. **2007**, *9*, 2525-2528.

2. Carbostannylation of alkynes

Carbostannylation of alkynes provides access to alkenyl stannanes. Shirakawa and Hiyama have extensively studied the potential of the transition metal-catalyzed carbostannylation of alkynes.[35] They found that alkynylstannanes could add to a carbon-carbon triple bond of various arylacetylenes, conjugated yonates, propargyl amines and ethers in the presence of palladium-iminophosphine complex (**37**) as catalyst (Scheme 25). Main products contained the stannyl group at a less hindered carbon atom, though the reaction of ynoates showed opposite regioselectivity.



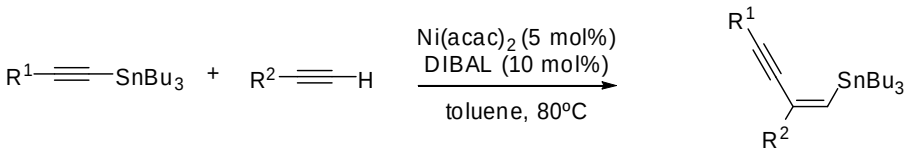
Scheme 25

Compared with other conventional phosphine ligands such as triphenylphosphine and 1,3-bis(diphenylphosphino)propane (DPPP), iminophosphine ligands were much more effective. The substituent on the nitrogen atom of iminophosphines largely affected the regioselectivity on alkynes: a cyclohexyl group at R was suitable for the reaction of arylacetylenes and propargyl amines and ethers, whereas conjugated yonates and yones preferred the iminophosphine with R = Ph.

A nickel complex also was able to catalyze the alkynylstannylation of alkynes (Scheme 26). It is noteworthy that the regioselectivity was perfect in contrast to the palladium-catalyzed alkynylstannylation that often gave mixtures of regioisomers. Internal alkynes did not yield products, contrary to reactions with the palladium catalyst. Although electron-deficient terminal alkynes were not suitable for the nickel catalyst, palladium could complement the reaction of such substrates.[36]

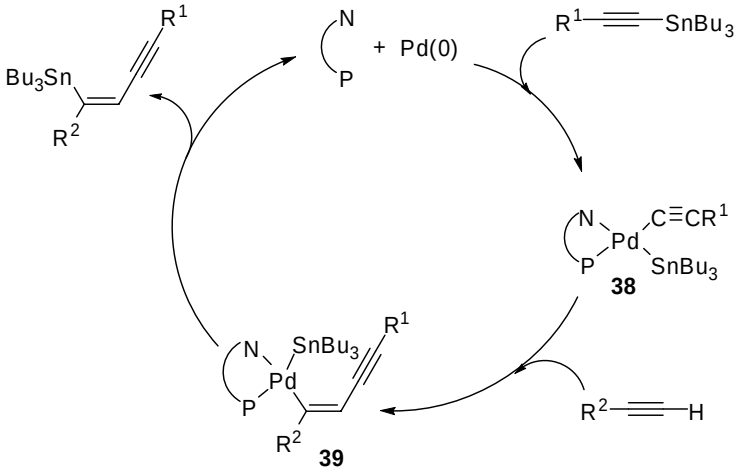
35 Shirakawa, E.; Hiyama, T. *J. Organomet. Chem*. **2002**, *653*, 114-121.

36 Shirakawa, E.; Yamasaki, K.; Yoshida, H.; Hiyama, T. *J. Am. Chem. Soc*. **1999**, *121*, 10221-10222.



Scheme 26

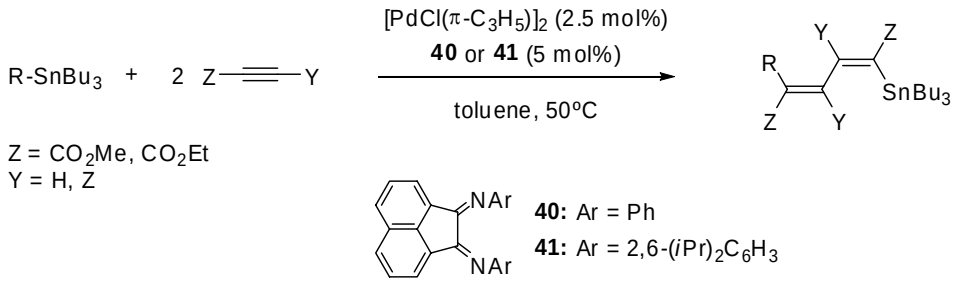
The palladium-catalyzed alkynylstannylation of alkynes is considered to be initiated by oxidative addition of an alkynylstannanes to a palladium(0) complex resulting Pd(II) complex **38**. Successive insertion of an alkyne into the C-Pd bond of **38** affords **39**. Finally reductive elimination from **39** furnishes the carbostannylation product and regenerates the Pd(0) complex (Scheme 27).



Scheme 27

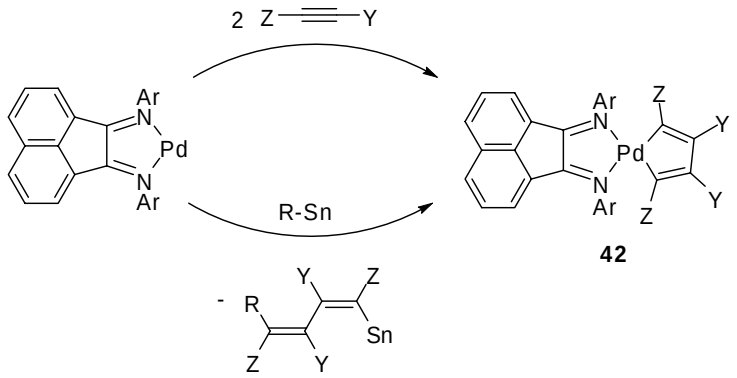
Use of bis(phenylimino)acenaphtene (**40**) instead of iminophoshine as ligand, changed the reaction course by formation of dimerization-alkynylstannylation products (Scheme 28).[37] The reaction was applicable not only to alkynylstannanes but also to alkenyl-, allyl- and arylstannanes, which upon reaction with ethyl propiolate or dimethyl acetylenedicarboxylate gave conjugated alkynylstannanes with high stereoselectivity. Although a mixture of regioisomers was produced in the reaction of ethyl propiolate with other organostannanes than alkynylstannanes, the more bulky diimine ligand (**41**) completely eliminates formation of minor isomers.

37 Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc*. **1999**, *121*, 4290-4291.



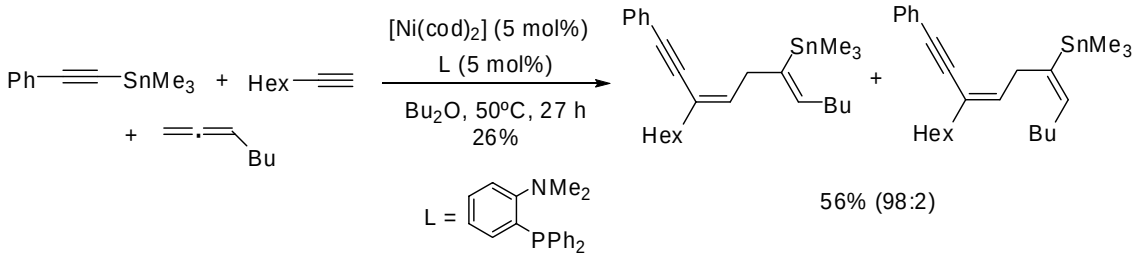
Scheme 28

Palladacyclopentadiene **42** is believed to be generated by oxidative cyclization between a palladium(0) complex and two molecules of alkyne, which was shown to be a key intermediate. Intermediate **42** reacts with organostannanes to give the dimerization-carbostannylation products exclusively.



Scheme 29

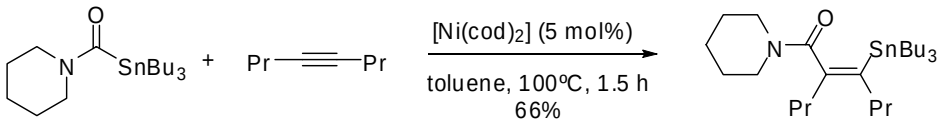
A tandem carbostannylation reaction with two sequential insertions of different C-C unsaturated bonds into a tin-alkynyl carbon bond was recently described.[38] Nickel was able to catalyze the assembly of alkynylstannanes, alkynes and 1,2-dienes into alkenylstannanes having a dienyne structure that is otherwise difficult to access by a direct route.



Scheme 30

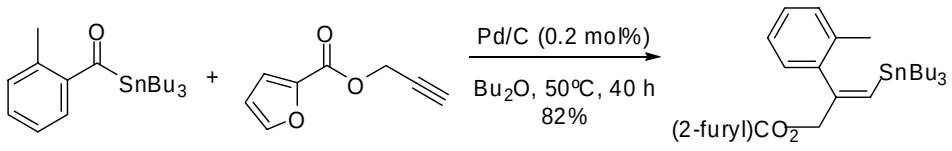
38 Shirakawa, E.; Yamamoto, Y.; Nakao, Y.; Shinichi, O.; Tsuchimoto, T.; Himaya, T. *Angew. Chem. Int. Ed*. **2004**, *43*, 3448-3451.

Acylstannanes could also be added to alkynes using [Ni(cod)$_2$] as catalyst (Scheme 31).[36,39] The reaction was applicable to aromatic and aliphatic acylstannanes in addition to aminocarbonylstannanes, which react with both electron-rich and -deficient alkynes. The stannyl group of acylstannanes attacks preferably an alkyne carbon having a more electron-withdrawing group. The catalytic cycle is proposed to start with oxidative addition of an acylstannane to a nickel(0) complex, followed by insertion of an alkyne and reductive elimination.



Scheme 31

Aryl-, alkenyl-, and alkylstannanes are less reactive because of their lower reactivity in the oxidative addition to low-valent transition-metal complexes. They could however undergo carbostannylation of alkynes through the decarbonylative addition of acylstannanes catalyzed by Pd/C (Scheme 32).[40] In the reaction, only one regio- and stereoisomer was observed.



Scheme 32

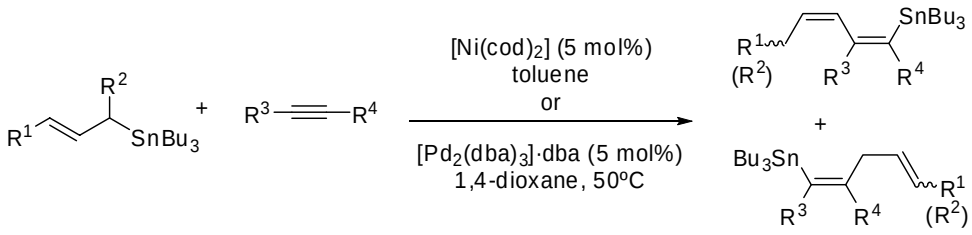
Various 1,4-dienylstannanes could be prepared by the nickel- or palladium-catalyzed allylstannylation of alkynes (Scheme 33).[36,41] The two catalysts complemented each other with regard to the electronic nature of the alkyne substrates. [Ni(cod)$_2$] was sensitive to the electronic character of a substituent on a carbon-carbon triple bond, and favoured regioselective attack of a stannyl group to an alkyne carbon having a more electron-withdrawing substituent. [Pd$_2$(dba)$_3$]·dba catalyzed the reaction without any phosphine or imine ligand in sharp contrast to the alkynylstannylation and

39 Shirakawa, E.; Yamamoto, Y.; Nakao, Y.; Tsuchimoto, T.; Hiyama, T. *Chem. Commun*. **2001**, 1926-1927.

40 Nakao, Y.; Satoh, J.; Shirakawa, E.; Himaya, T. *Angew. Chem. Int. Ed*. **2006**, *45*, 2271-2274.

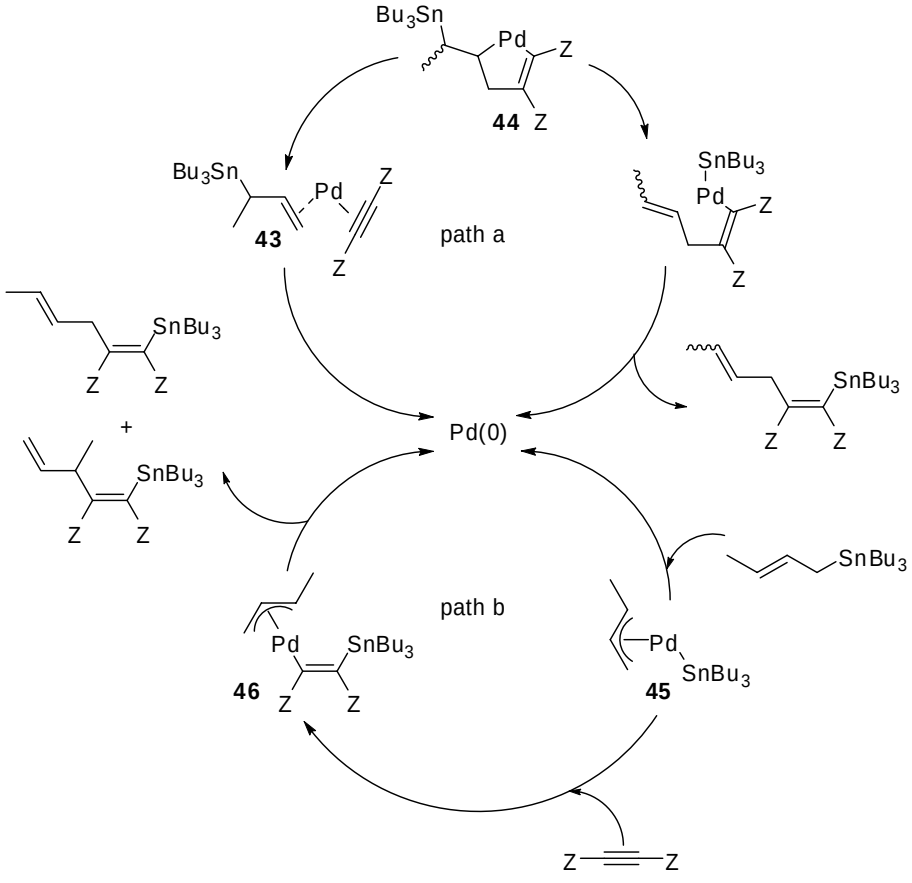
41 Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *Org. Lett*. **2000**, *2*, 2209-2211.

dimerization-carbostannylation, which, respectively, required an iminophosphine or diimine ligand.



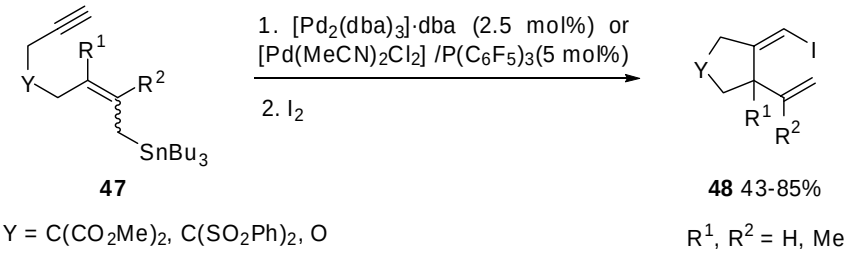
Scheme 33

The palladium-catalyzed allylstannylation of alkynes was proposed to proceed by oxidative cyclometalation on an alkene-alkyne palladium complex **43** to form a palladacyclopentene **44**, which would undergo β-tin elimination, followed by reductive elimination (path a). An alternative mechanism (path b) would involve oxidative addition of the allyltin reagent to a Pd(0) complex to give a (η^3-allyl)palladium intermediate (**45**). This complex undergoes insertion of the alkyne to produce (η^3-allyl)palladium (**46**). Reductive elimination provides the final products (Scheme 34).



Scheme 34

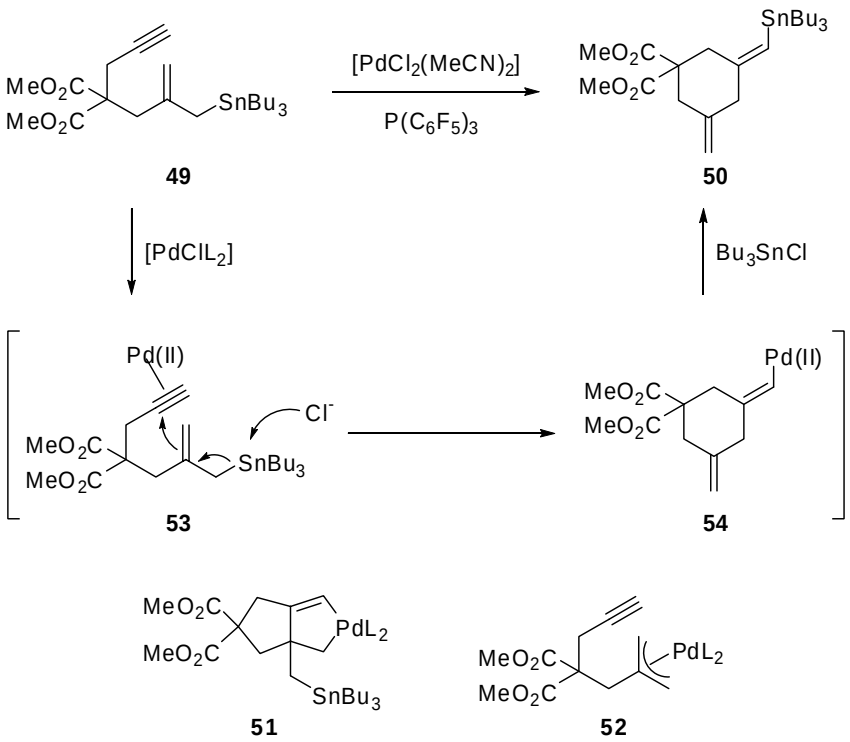
The intramolecular version of this reaction was studied in our research group (Scheme 35).[42] It was found that substrates of type **47** undergo cyclization with Pd(0) or Pd(II) catalysts in a stereoselective process. Since the final stannanes suffered partial protodestannylation, usually the products were treated with I_2 and the corresponding alkenyl iodides were isolated with retention of configuration at the exocyclic double bond. The reactions afforded stereoselectively carbocycles **48**, which showed a *Z* configuration at the alkene. These results were consistent with a Pd(0) catalyzed reaction following the possible pathways proposed by Shirakawa.[41]



Scheme 35

Interestingly, substrate **49** gave exclusively the six-membered carbocycle **50** with the opposite alkene configuration (Scheme 36). The possible intermediates that could be formed by reaction of **49** with a Pd(0) active catalyst (**51** or **52**) cannot evolve by the pathway outlined in Scheme 34, since neither β-tin elimination nor insertion of the alkyne (due to geometrical constraints) can occur. For this reaction it was proposed the Pd(II)-catalyzed process outlined in Scheme 36. Here, the formation of the C-C bond occurs by nucleophilic anti attack of the stannane on the (η^2-alkyne)palladium(II) complex, as shown in **53**, to give intermediate **54**. Cleavage of the Pd-C bond by electrophilic Bu_3SnCl affords the final product.

42 Martín-Matute, B.; Buñuel, E.; Méndez, M.; Nieto-Oberhuber, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Organomet. Chem*. **2003**, *687*, 410-419.



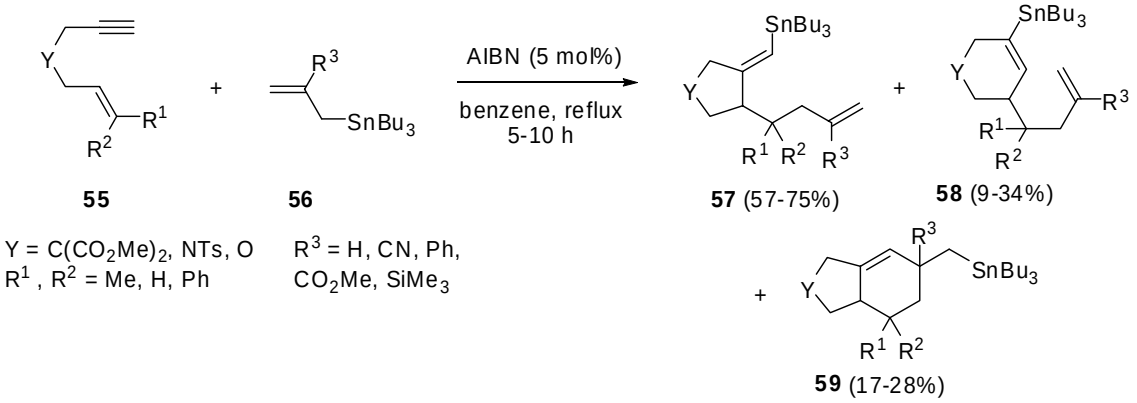
Scheme 36

This *anti* attack of the allylstannane to an (η^2-alkyne)metal complex was the reaction pathway observed for the same reaction catalyzed by several electrophilic metals such as Pt(II), Ru(II), Ag(III), Cu(I).[43] In this case, the reactions were performed in MeOH and the isolated products where those arising from protodemetalation of the alkenylmetal intermediate.

The actual reaction pathway of the Pd(0) catalyzed reaction was studied by DFT calculations.[42] The results supported a mechanism for the allylstannylation of alkynes consisting in Sn-C oxidative addition of the allylstannane to a Pd(0) precursor affording a (η^3-allyl)palladium complex (path b in Scheme 34). In the lowest energy pathway, the alkyne ligand would coordinate after the oxidative addition, then insertion into the Pd-Sn bond. Reductive elimination of the final product would re-generate the active Pd(0) catalyst.

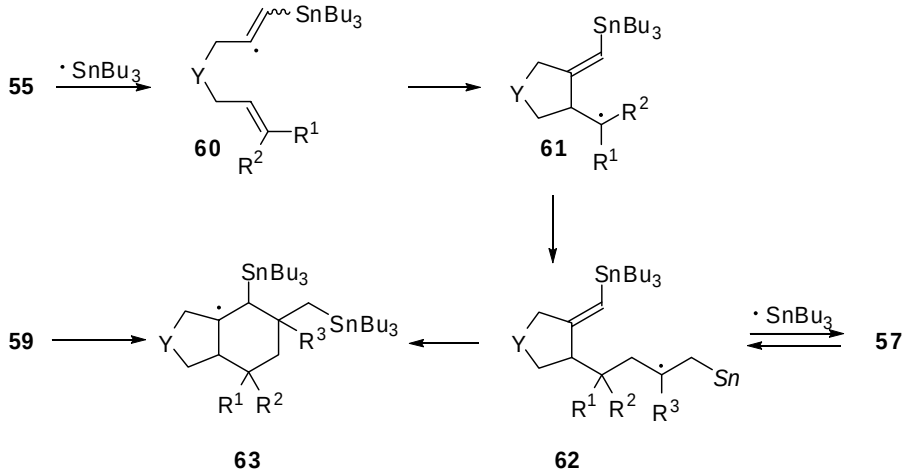
43 (a) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222. (b) Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem*. **2002**, *123*, 8416-8417.

Another approach to perform the allylstannylation of alkynes consists of a radical process.[44] Hosomi and co-workers reported the formation of alkenylstannanes **57** from enynes **55** in the presence of allylstannanes **56** (Scheme 37). Together with **57**, six-membered ring products **58** and bicycles **59** were formed in some cases as minor compounds.



Scheme 37

The reaction was not highly diastereoselective with the major diastereomer having an *E* configuration at the double bond of **57** (d.r. = 61:39-86:14). The proposed mechanism for the cyclization is shown in Scheme 38.



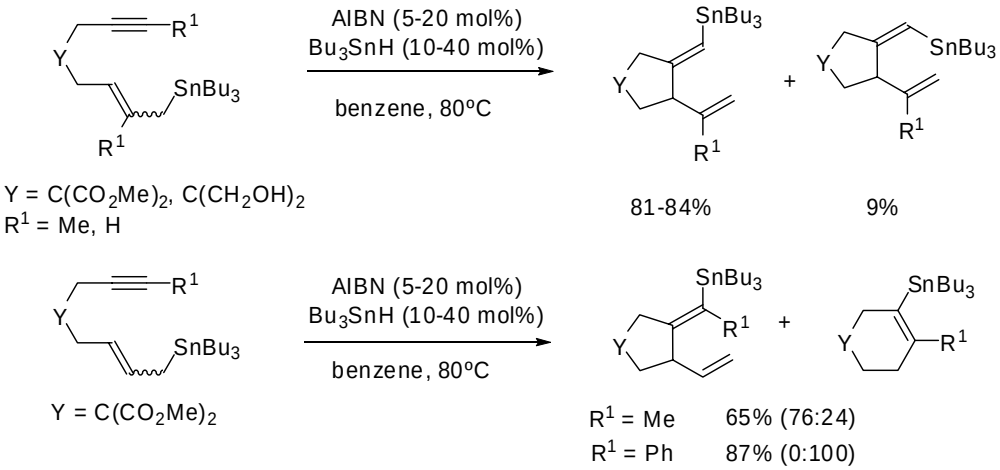
Scheme 38

Intermolecular addition of $\cdot SnBu_3$, generated from the allylstannane, to the alkyne affords the radical intermediate **60**, which undergoes cyclization to furnish **61**. Addition of this radical to a molecule of allylstannane provides **62** which suffers homolytic rupture to give **57** and regenerate $\cdot SnBu_3$. The formation of byclicles

44 (a) Miura, K.; Matsuda, T.; Hondo, T.; Ito, H.; Hosomi, A. *Synlett*, **1996**, 555-556. (b) Miura, K.; Itoh, D.; Hondo, T.; Saito, H.; Ito, H.; Hosomi, A. *Tetrahedron Lett*. **1996**, *37*, 8539-8542. (c) Miura, K.; Saito, H.; Fujisawa, N.; Hosomi, A. *J. Org. Chem*. **2000**, *65*, 8119-8122.

compounds (**59**) could be rationalized by intramolecular homolytic substitution of **62** via **63**. Six membered-ring compounds **58** were formed by addition of the tributylstannyl radical to the internal sp-carbon in **55**.

The intramolecular version of the allylstannylation was described using allylstannanes-alkynes as depicted in Scheme 39.[45] To achieve good yields it was necessary to add 10-40 mol% of Bu_3SnH, which promoted the radical formation step by increasing the concentration of $\cdot SnBu_3$. Non-terminal alkynes (R^1 = Me) afforded mixtures of *exo* and *endo* cyclizated products; for R^1 = Ph, only the *endo* regioisomer was observed in 87% yield.

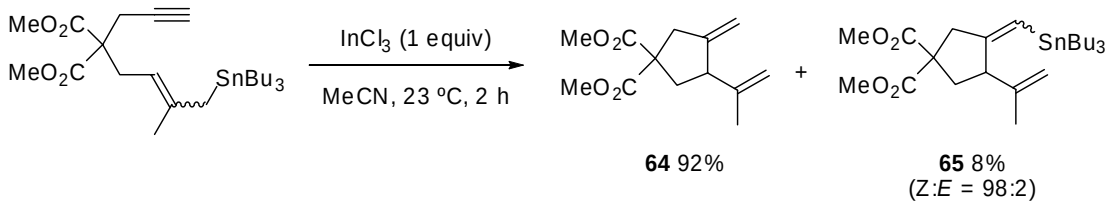


Scheme 39

Equimolar amounts of $InCl_3$ also promote the intramolecular allylation of alkynes with allylstannanes in the presence of AIBN.[46] In this case, the allylstannylation products **65** were obtained as minor compounds together with carbocycles **64** (Scheme 40). The proposed reaction mechanism for this transformation involved allylindation with an allylindium intermediate arising from the allylstannane moiety rather than its nucleophilic addition to an alkyne-$InCl_3$ complex. $GaCl_3$, as well as $InCl_3$, worked as good promoter for the cyclization reaction.

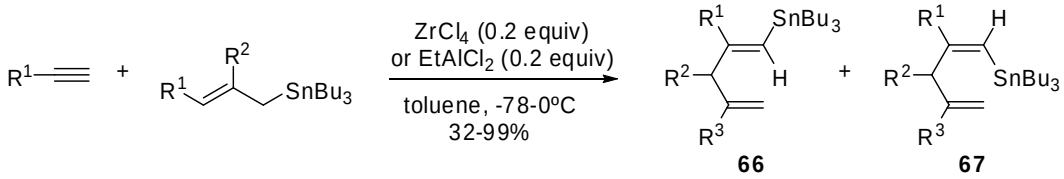
45 Miura, K.; Fijisawa, N.; Saito, H.; Nishikori, H.; Hosomi, A. *Chem. Lett*. **2002**, 32-33.

46 Miura, K.; Fujisawa, N.; Hosomi, A. *J. Org. Chem*. **2004**, *69*, 2427-2430.



Scheme 40

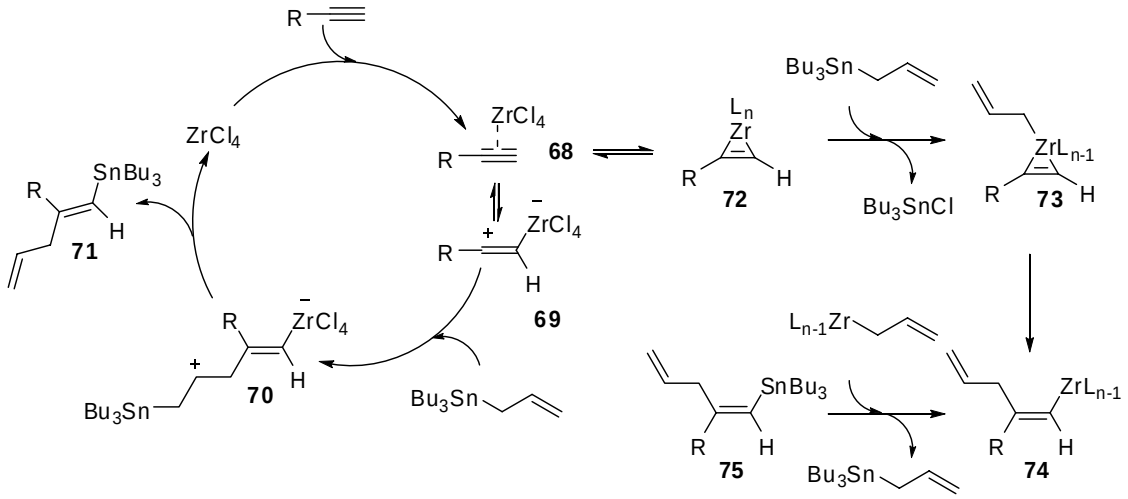
Along with the above methods to perform allylstannylations of alkynes, Lewis acids have also been used to catalyze this transformation (Scheme 41).[47] The addition of allylstannanes to alkynes proceeds in *trans* or *cis* fashion depending on the alkyne and the reactions conditions employed. Thus, when treated with catalytic amounts of $ZrCl_4$ (0.2 equiv) or $EtAlCl_2$ (0.2 equiv) in toluene, aromatic acetylenes afforded *trans*-adducts **66** while aliphatic acetylenes gave mixture of *trans*- and *cis*-adducts **67**. In the absence of solvent allylstannanes were added to aliphatic acetylenes in a *trans*-fashion.



Scheme 41

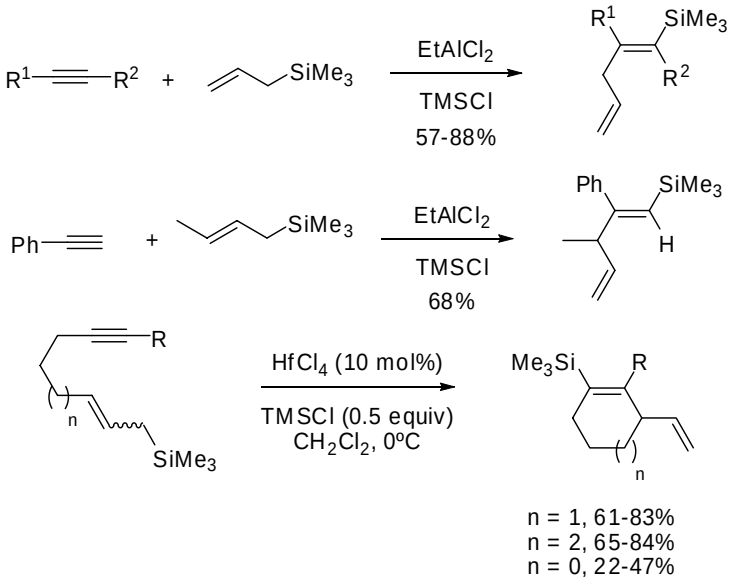
The proposed mechanism is shown in Scheme 42 for $ZrCl_4$. The *trans*-stannylation involved the coordination of metal to the alkyne to produce π-complex **68**, which would be stabilized by the π-system of R group in the case of aromatic acetylenes to form the zwitterionic intermediate **69**. Allylstributylstannane could attack the electro-deficient carbon from the side opposite to the Lewis acid to produce adduct **70** stereoselectively, which would undergo elimination of Bu_3Sn^+. Transmetalation of zirconium halide by the tributylstannyl group would afford the *trans*-allylstannylated product **71** and regenerate the catalyst. On the other hand, aliphatic alkynes might produce the η^2-complex **72** because the corresponding stabilization of vinyl cation by a π-system is not possible. Allyltributylstannane would react with (ZrL_n) of **72** to form allylzirconium **73**, which would undergo the regioselective intramolecular allylation to give the vinylzirconium derivative **74**. Transmetalation of zirconium halide by the tributystannyl group would afford the *cis*-allylstannylated product **75**.

47 Matsukawa, Y.; Asao, N.; Kitahara, H.; Yamamoto, Y. *Tetrahedron Lett*. **1999**, *55*, 3779-3790.



Scheme 42

Lewis acids not only promote allylstannylation of alkynes. Allylsilylation was also reported to proceed in good yield with Lewis acids to afford the *trans*-allylated compounds as sole regioisomers (Scheme 43).[48] The carbosilylation was applicable to crotyltrimethylsilane, furnishing the γ-addition product without any trace of the α-addition. Besides, strong Lewis acids such as HCl_4 were found to promote the intramolecular allylsilylation of unactivated alkynes, proceeding exclusively in the *endo*-fashion to give five-, six-, and seven-membered carbocycles in moderate to high chemical yields.[49]



Scheme 43

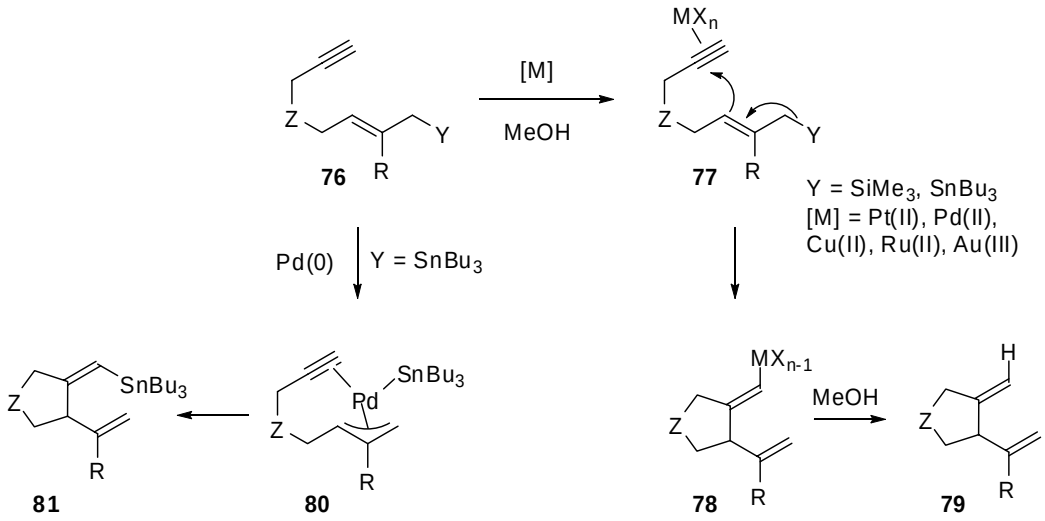
48 Asao, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem*. **1996**, *61*, 4874-4875.

49 Imamura, K.-I.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc*. **1998**, *120*, 5339-5340.

Chapter 2. Objectives

Objectives

Metal-catalyzed cyclizations by intramolecular attack of allylsilanes or allylstannanes onto alkynes have previously been studied in our research group.[42,43] In the presence of a protic solvent and electrophilic metal catalysts, cyclizations of substrates **76** (Y = $SiMe_3$, $SnBu_3$) afforded hetero- or carbocycles **79** (Scheme 44). The reaction mechanism involved an *anti* attack of the allylstannane in **77** to the (η^2-alkyne)metal complex to form an alkenyl metal **78**, which after protonolysis afforded **79**. On the other hand, when the reactions of substrates **76** (Y = $SnBu_3$) were catalyzed by Pd(0) complexes, stannyl derivatives **81** were obtained stereoselectively. In this case, the reaction proceeded via a (η^3-allyl)palladium intermediate (**80**) to give **81**.



Scheme 44

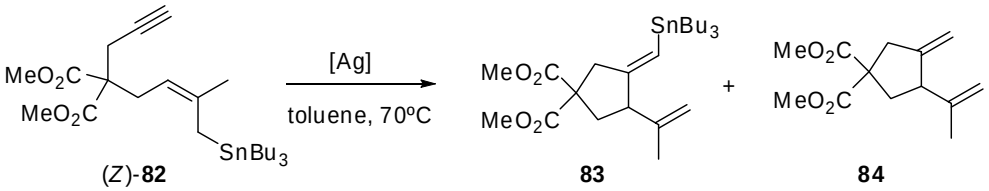
Taking advantage of the structural diversity offered by cycloisomerization reactions of activate alkynes, we aimed to find new metals that afforded different cyclization modes of substrates **76**. Since alkenylstannanes have significant synthetic potential as precursors for the construction of functionalized molecules, we were interested in obtaining cycloisomerizated products where the stannane functionality remains attached to the final product.

Chapter 2. Results and Discussion

1. Intramolecular carbostannylation of alkynes catalyzed by silver (I)

Silver-catalyzed reactions have recently begun to emerge as important methods for organic synthesis. As it was shown in the introduction, silver(I) has been used to activate alkynes based on both the Lewis acidity and the transition metal character of the silver catalyst. For this reason, we decided to test the activity of various silver salts in the cyclization of allylstannanes-alkynes. Compound (*Z*)-**82** was chosen as a model for these reactions.

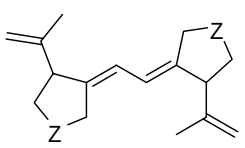
Table 1: Silver(I)-catalyzed carbostannylation of **82**.



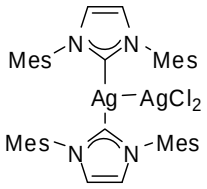
(*Z*)-**82** **83** **84**

Entry	[Ag] (mol%)	Time	Yield of **83** (%)	Yield of **84** (%)
1[a]	AgOTf (10)	12 h	29	24
2[a]	$AgBF_4$ (10)	12 h	29	-[b]
3	AgO_2CCF_3 (10)	12 h	-	-
4	**86** (5)	12 h	-	-
5	$AgSbF_6$ (10)	1 min	83	12
6	AgOTf (10) + PPh_3 (10)	10 min	91	-
7	$AgSbF_6$ (10) + PPh_3 (10)	1 min	83	5
8	AgOTf (10) + (±)-binap (5)	5 min	86	4
9	$[AgOTf(PPh_3)]_3$ (3)	30 min	90	-

(a) Conversion of 85%. (b) Dimer **85** (7%) was obtained. Tf = trifluoromethanesulfonyl, Mes = 2,4,6-trimethylphenyl.



85: Z = $C(CO_2Me)_2$

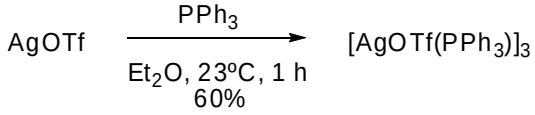


86

AgOTf, which is one of the most commonly used salts in silver catalyzed transformations,[22-26,30,34] gave stannane **83** in 29% yield along with the destannylated

analogue **84** in 24% yield (Table 1, entry 1). Although the yields were low and both compounds result from a 5-*exo*-*dig* cyclization as was observed before,[42,43] the major compound **83**, retained the stannane unit. The use of $AgBF_4$ led to **83** and dimer **86** in low yield, whereas AgO_2CCF_3 and complex **86** were ineffective (Table 1, entries 2, 3 and 4). Remarkably, $AgSbF_6$ led to a very fast cyclization of (Z)-**82** and yielded **83** (83%) and **84** (12%). Lowering the reaction temperatures with the latter catalyst, enhanced the amount of destannylated product **84** and the reaction times.

The effect of adding different phosphines in the reaction medium was also investigated. The addition of 10 mol% of triphenylphosphine to AgOTf improved the chemical yield significantly up to 91% (Table 1, entry 6), while in the case of $AgSbF_6$ it did not have a significant effect (Table 1, entry 7). The reaction also proceeded well in the presence of a variety of silver(I) complexes generated *in situ* bearing phosphines as ligands: [Ag(OTf)L] (L= (*o*-tolyl)$_3$P, (naphthyl)$_3$P, (Cy)$_2$[(*o*-Ph)C$_6$H$_4$]P or [(AOTf)$_2$(L-L)] (L-L = ethane-1,2-diylbis(diphenylphosphane) (dppe), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (xantphos), 1,1'-binaphtyl (binap). Among those phosphines, binap gave the reaction in 85-91% yield (Table 1, entry 8).[50,51] No reaction was observed when the ratio of L to Ag was higher than 1:1. Reaction with the preformed complex [AgOTf(PPh$_3$)$_3$][52] prepared as depicted in Scheme 45, also gave **83** in good yield (Table 1, entry 9).



Scheme 45

42 Martín-Matute, B.; Buñuel, E.; Méndez, M.; Nieto-Oberhuber, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Organomet. Chem*. **2003**, *687*, 410-419.

43 (a) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222. (b) Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem*. **2002**, *123*, 8416-8417.

50 (a) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc*. **2005**, *127*, 14556-14557. (b) Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc*. **2004**, *126*, 5360-5361. (c) Wadamoto, M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem*. **2003**, *68*, 5593-5601. (d) Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc*. **1996**, *118*, 4723-4724.

51 Denmark, S. E.; Fu, J. *Chem. Rev*. **2003**, *103*, 2763-2793.

52 Bajardí, M.; Crespo, O.; Laguna, A.; Fishcer, K. *Inorg. Chim. Acta* **2000**, 304-7-16.

A series of allylstannanes-alkynes were prepared in order to examine the scope of this catalytic process. Substrates (*E*)-**82**, **87**, (*Z*)-**88**, (*E*)-**88**, and **89** (Figure 3) were obtained by propargylation of the corresponding stannanes with propargyl bromide and NaH. The stannanes were prepared as was described in Chapter 1.

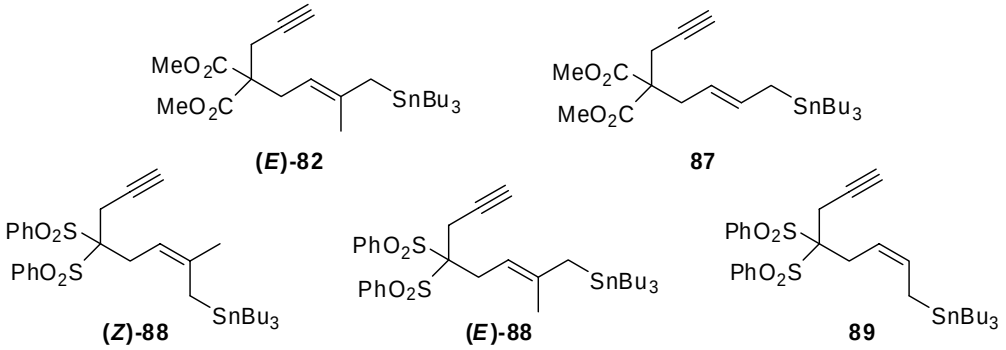
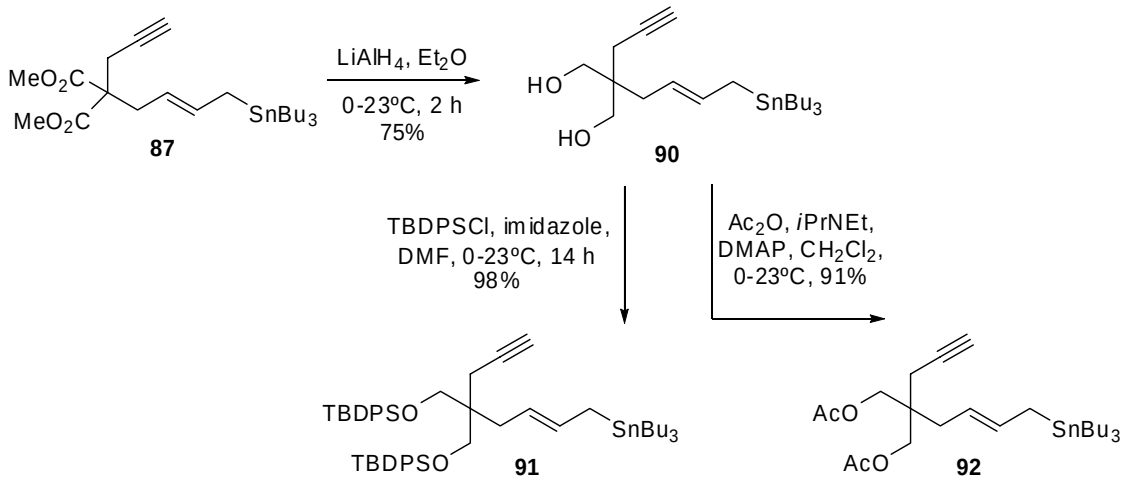


Figure 3

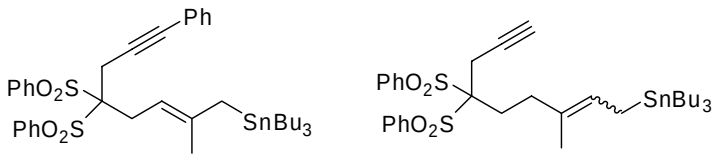
Reduction of the malonate at the tether of **87** with $LiAlH_4$ afforded diol **90**,[46] which by reaction with *tert*-butyldiphenylsilyl chloride or acetic anhydride afforded the silyl protected diol **91** and the diacetate **92**, respectively.



Scheme 46

Compound **93**, with an internal alkyne, and compound **94**, with an additional methylene at the stannane chain (Figure 4), were prepared by alkylation of (*E*)-5,5-bis(phenylsulfonyl)-3-methyl-2-penten-1-yl-tri-*n*-butylstannane and 6,6-bis(phenylsulfonyl)-3-methyl-1-(tri-*n*-butylstannyl)-2-hexene, with (3-bromo-1-propynyl)benzene and propargyl bromide, respectively.

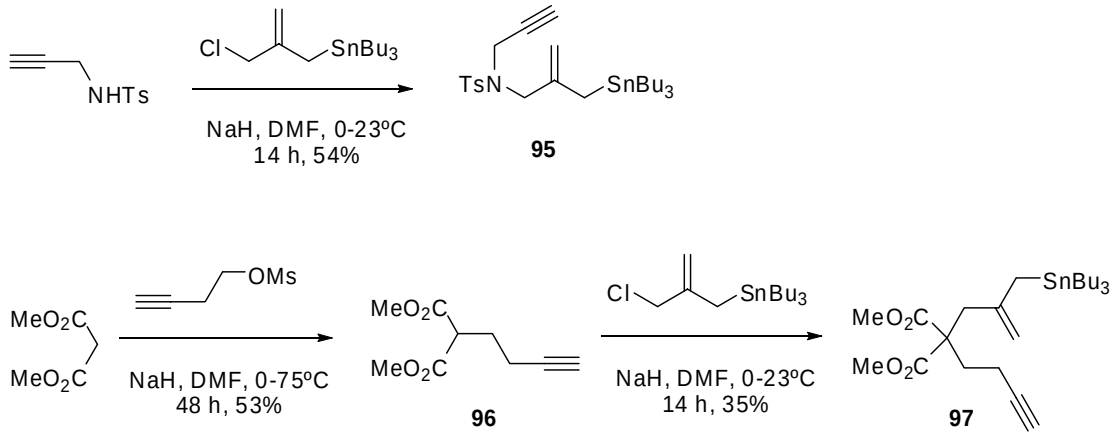
46 Miura, K.; Fujisawa, N.; Hosomi, A. *J. Org. Chem*. **2004**, *69*, 2427-2430.



93 **94**

Figure 4

Stannane **95** with a tosylamide at the tether was prepared by alkylation of *N*-2-propynyl-(4-toluene)-sulfonamide[53] with 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene.[54] Stannane **97**, with and additional methylene at the alkyne chain, was prepared by alkylation of dimethyl malonate with 3-butyn-1-yl mesylate[55] to afford **96**, which after a second alkylation with 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene furnished **97** (Scheme 47).



Scheme 47

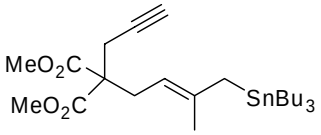
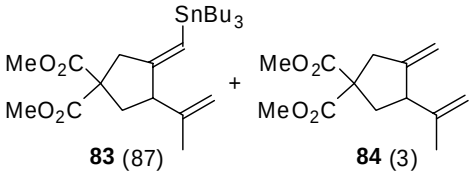
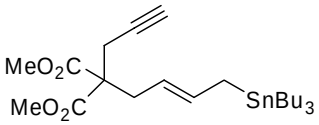
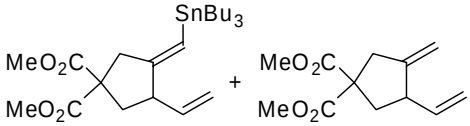
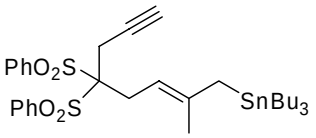
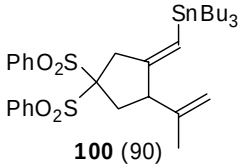
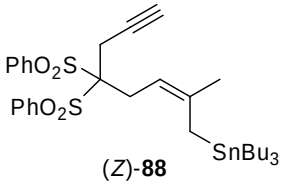
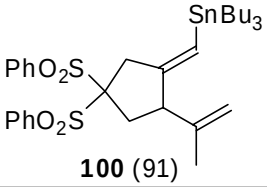
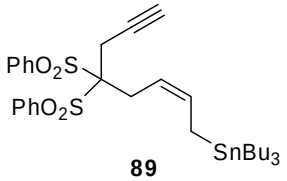
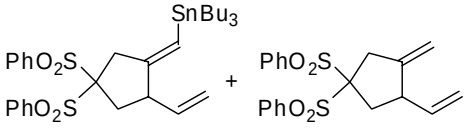
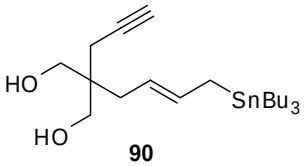
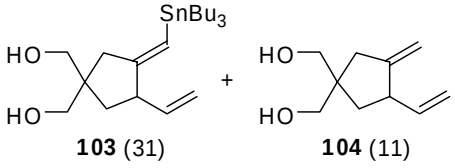
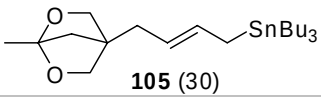
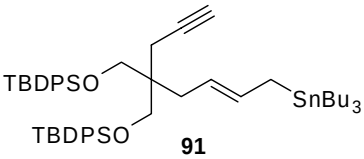
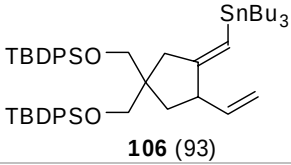
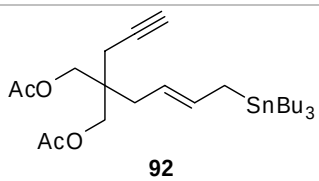
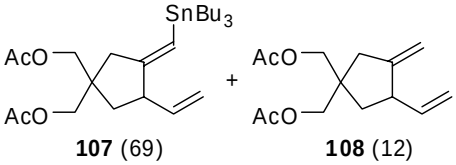
These substrates were subjected to reaction with $[AgOTf(PPh_3)]_3$ (3 mol%) in toluene at 70ºC. Although $AgSbF_6$ was shown to be more reactive than $[AgOTf(PPh_3)]_3$ (Table 1, entries 5 and 9), the amount of destannylated compound observed using this catalyst was lower. In addition, $[AgOTf(PPh_3)]_3$ is less air sensitive than $AgSbF_6$.

53 Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C. Y. *Tetrahedron Lett*. **1988**, *29*, 6433-6436.

54 Keck, G. E.; Yu, T.; McLaws, M. D. *J. Org. Chem*. **2005**, *70*, 2543-2550.

55 Casey, C. P.; Dzwiniel, T. L.; Kraft, S.; Guzei, I. A. *Organometallics* **2003**, *22*, 3915-3920.

Table 2: Silver(I)-catalyzed carbostannylation of (*E*)-**82**, **87**-**92**.[a]

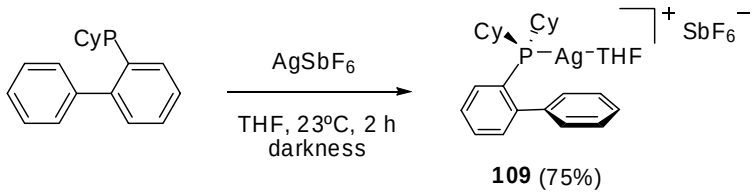
Entry	Substrate	Time (h)	Product(s) (Yield, %)
1	 (*E*)-**82**	0.5	 **83** (87) + **84** (3)
2	 **87**	5	 **98** (71) + **99** (6)
3	 (*E*)-**88**	0.5	 **100** (90)
4	 (*Z*)-**88**	0.5	 **100** (91)
5	 **89**	3.5	 **101** (72) + **102** (9)
6	 **90**	0.2	 **103** (31) + **104** (11)  **105** (30)
7	 **91**	2	 **106** (93)
8	 **92**	2.5	 **107** (69) + **108** (12)

(a) Reaction with $[AgOTf(PPh_3)]_3$ (3 mol%) in toluene at 70ºC.

The reaction of substrates similar to (*Z*)-**82** proceeded satisfactorily regardless of their *E*/*Z* configuration. For example, (*E*)-**82** (Table 2, entry 1) reacted similarly to (*Z*)-

82, and both (*Z*)-**88** and (*E*)-**88** gave **100** in 90-91% yields after 30 minutes (Table 2, entries 3 and 4). Substrates in which the olefin at the allylstannane chain is only disubstitued gave slightly lower yields and needed longer reaction times than those in which the olefin is trisubstituted (Table 2, entries 2 and 5). The reaction tolerated protection of the hydroxy groups with acetate and *tert*-butyldiphenylsilyl groups (Table 2, entries 7 and 8). The free hydroxy groups in substrate **90** competed in the reaction with the alkyne, leading to a 1:1 ratio of bicyclic acetal **105** and stannane **103** (Table 2, enty 6). A similar cyclization of diols with alkynes has been reported by Genêt and co-worker with gold(I) catalysts.[56]

The cyclization of **93**, **94**, **95** and **97** failed with both $[AgOTf(PPh_3)]_3$ and $AgSbF_6$. Complex $[AgOTf(PPh_3)]_3$ was inactive even at temperatures over 70ºC, while $AgSbF_6$ was transformed to Ag(0) after longer reaction times. We observed that the addition of a bulky phosphine ($(Cy)_2[(o\text{-}Ph)C_6H_4]P$) in the presence of $AgSbF_6$ prevented the deposition of Ag(0) and yielded the desired products. The complex formed by reaction of $(Cy)_2[(o\text{-}Ph)C_6H_4]P$ with $AgSbF_6$ (**109**) was isolated as depicted in Scheme 48.



109 (75%)

Scheme 48

The structure of complex **109** was confirmed by X-ray crystal structure determination (Figure 5). It has the same structure in the solid state than related cationic gold(I) complexes previously described in our group.[57] Comparing the more significant distances, the Ag-P length (2.34 Å) was longer than in the case of the cationic gold(I) complex with the same phosphine (Ag-P, 2.24 Å). The bending of the P-Ag-THF angle (174.50º) was similar to that found for gold (P-Au-NCMe angle = 174.43º) and the distances Ag-C7/C8/C12 (3.04, 3.17, 3.29 Å) were also similar to the values obtained for gold (Au-C7/C8/C12 = 3.02/3.25/3.24 Å).

56 Antoniotti, S.; Genin, E.; Michelet, V.; Genêt, J.-P. *J. Am. Chem. Soc*. **2005**, *127*, 9976-9977.

57 Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2006**, *45*, 5455-5459.

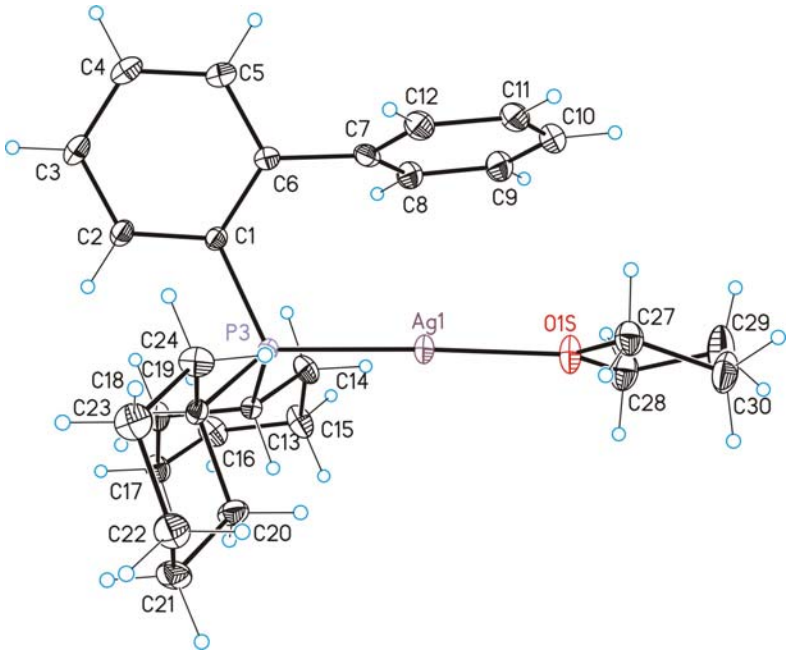
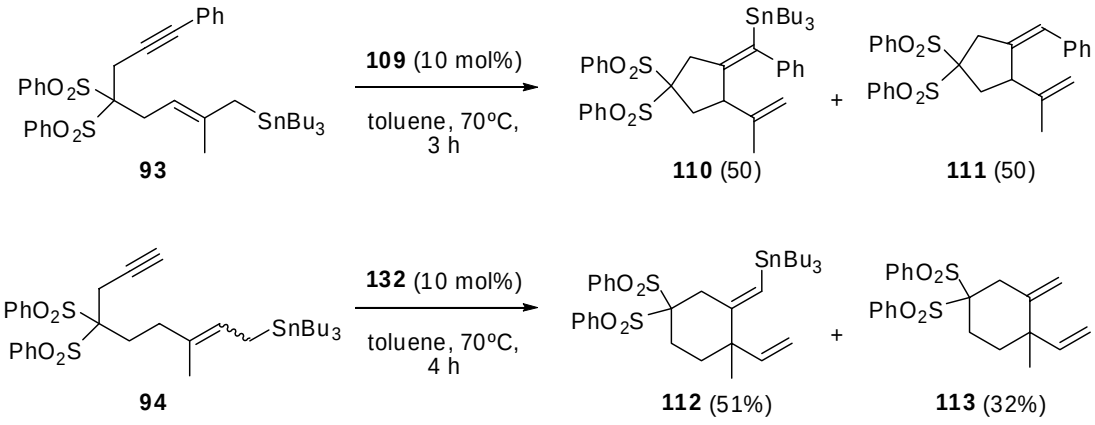


Figure 5. X-ray crystal structure of the cation silver(I) complex **109**.

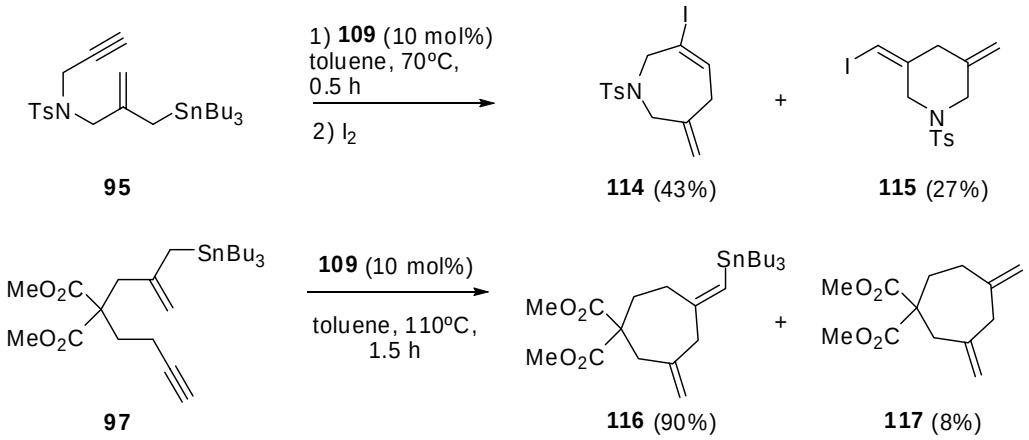
Applying complex **109** as catalyst in the intramolecular carbostannylation reaction of substrates **93**, **94**, **95**, and **97** led to smooth cyclizations as is shown in Schemes 49 and 50. Substrate **93**, which is substituted at the alkyne with a phenyl group, reacted with catalyst **109** to give a 1:1 ratio of **110** and **111** in quantitative yield. In this case, extensive destannylation of **110** was observed, probably during the chromatography. The reaction could be extended to the preparation of six-membered-ring compounds. Thus, substrate **94**, with an additional methylene group at the stannane chain, afforded the six-membered-ring derivatives **112** and **113**.



Scheme 49

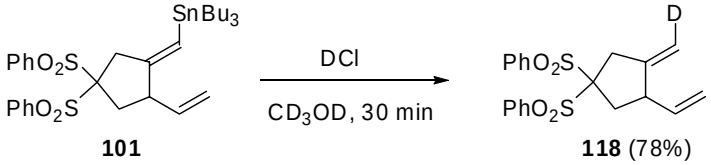
A 7-*endo-dig* cyclization was the predominant pathway in the reaction of tosylamide **95**, which afforded heterocycle **114** as the major product after treatment of

the mixture of stannanes with I_2. In this case, treatment with I_2 was necessary to achieve a good chromatography separation of the both compounds formed. A seven-membered ring **116** was also obtained in good yield in the 7-*exo-dig* cyclization of **97**.



Scheme 50

In all cases, the alkenyl stannanes were obtained as single stereoisomers, whose configuration was assigned as *E* by comparison of their spectra with those of the *Z* isomers obtained in the cyclization catalyzed by Pd(0).[42] Analysis of the NOESY spectrum of the deuterated compound **118**, prepared by reaction of stannane **101** with DCl in CD_3OD (Scheme 51), confirmed the *E* configuration at the double bond.

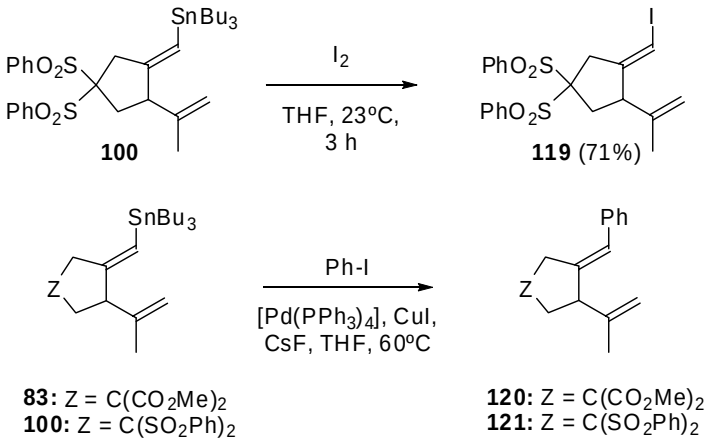


Scheme 51

The utility of this intramolecular carbostannylation reaction was demonstrated by transformation of the formed (*E*)-alkenyltin compounds (Scheme 52) to the alkenyl iodides and their use in the Stille coupling reaction. The iodolysis of **100** afforded the corresponding alkenyl iodide **119** in a good yield. Although sterically hindered, the alkenylstannanes **83** and **100** were good substrates for Stille reactions with iodobenzene. In the presence of [$Pd(PPh_3)_4$] (10 mol%), CuI (10 mol%), and CsF (4 equiv) in THF[58] **120** and **121** were obtained stereospecifically. Compound **121** was the *E* diastereomer of

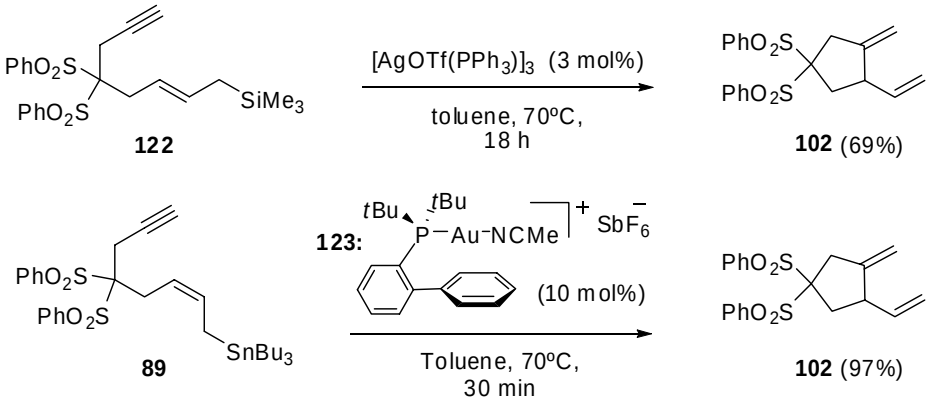
58 (a) Mee, S. P. H.; Lee, V.; Baldwin, J. E. *Angew. Chem. Int. Ed*. **2004**, *43*, 1132-1136. (b) Mee, S. P. H.; Lee, V.; Baldwin, J. E. *Chem. Eur. J*. **2005**, *11*, 3294-3308.

111 (Scheme 49), thus providing further confirmation of the configuration assigned to the alkenylstannanes obtained.



Scheme 52

Reaction of allylsilane **122** using $[AgOTf(PPh_3)]_3$ as catalyst led only to destannylated product **102** after 18 h at 70ºC (Scheme 53). The same destannylated product was the sole compound observed when allylstannane **89** was treated with the cationic gold(I) complex **123**[57] in toluene for 30 min.



Scheme 53

2. Enantioselective intramolecular carbostannylation of alkynes

The good yields obtained in the cyclization of (*Z*)-**82** with AgOTf using (±)-binap as ligand for the catalysis (Table 1, entry 8), encouraged us to examine the enantioselective cyclization of allylstannanes with alkynes.[59] Thus, substrate (*E*)-**88** was subjected to the cyclization reaction using the chiral phosphines depicted in Figure 6.

59 For enantioselective cyclizations of enynes initiated by the coordination of the metal to the alkyne function of enynes, see: platinum(II) catalysis: (a) Charruault, L.; Michelet, V.; Taras, R.; Gladialli,

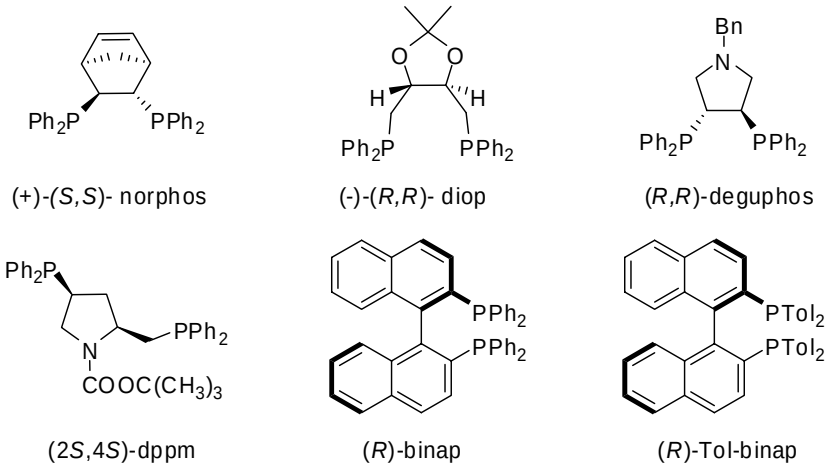


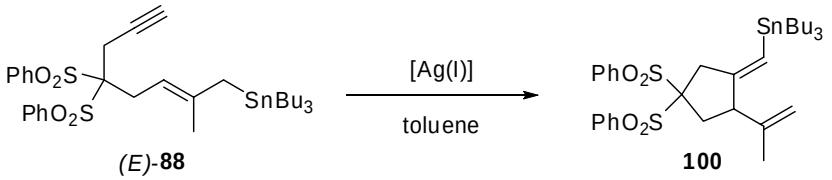
Figure 6

Bidentade ligands such us (+)-(*S*,*S*)-norphos, (-)-(*R*,*R*)-diop, (*R*,*R*)-deguphos, (2*S*,4*S*)-bppm in combination with AgOTf gave low enantiomeric ratios (e.r.) ranging from 53:47 to 63:37 (Table 3, entries 1-4). The best results were obtained when isolated complexes [$(AgOTf)_2$(*R*)-binap] or [$(AgOTf)_2$(*R*)-Tol-binap] were employed. These complexes were synthesized following a described procedure as shown in Scheme 54.[10b] (*R*)-Tol-binap gave a slightly better e.r. than (*R*)-binap under the same reaction conditions (Table 3, entries 9 and 10).

It was found that the nature of the counteranion played a crucial role. For example, no enantioselectivity was achieved with complex [$(AgSbF_6)_2$(*R*)-binap] (Table 3, entry 6), but the use of OTf, which is a better coordinating anion, led to a 89:11 e.r. under the same reaction conditions (Table 3, entry 7). The reaction performed by mixing $AgPF_6$, (*R*)-Tol-binap and the substrate, led also to a low enantioselectivity (68:32 e.r.) (Table 3, entry 5), whereas the same reaction with $AgBF_4$ gave only the destannylated product **124**. The temperature also affected the e.r. values. Thus, lowering the temperature from 70ºC to 50ºC, the e.r. increased from 87:12 to 89:11 (Table 3 entries 8 and 10). At 30ºC the e.r. did not improved and the reaction time was longer (Table 3, entry 7). Reaction of (*Z*)-**88** under the same reaction conditions as in entry 8 led to stannane **100** with a slightly diminished e.r. (80:19).

S.; Genêt, J.-P. *Chem. Commun*. **2004**, 850-851. (b) gold(I) catalysis: Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometallics* **2005**, *24*, 1293-1300.

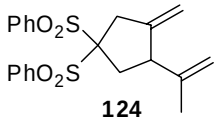
Table 3: Enantioselective cyclization of (*E*)-**88**.[a,b]



(*E*)-**88** **100**

Entry	[Ag(I)]	T (ºC)	Yield (%)[c]	e.r.[d]
1	AgOTf/(+)-(*S*,*S*)-norphos	70	n.d.	53:47
2	AgOTf/(-)-(*R*,*R*)-diop	70	n.d	53:47
3	AgOTf/(*R*,*R*)-deguphos	70	n.d.	42:58
4	AgOTf/(2*S*,4*S*)-bppm	70	n.d.	37:63
5	$AgPF_6$/(*R*)-Tol-binap[e]	30	n.d.	68:32
6	[$(AgSbF_6)_2$(*R*)-Tol-binap]	30	57	50:50
7[e]	[$(AgOTf)_2$(*R*)-Tol-binap]	30	74	89:11
8	[$(AgOTf)_2$(*R*)-Tol-binap]	50	91	89:11
9	[$(AgOTf)_2$(*R*)-binap]	70	87	86:13
10	[$(AgOTf)_2$(*R*)-Tol-binap]	70	87	87:12

(a) Reactions with non isolated complexes: 20 mol% of AgOTf and 10 mol% of L-L for 30 min. (b) Reactions with isolated complexes: 5 mol% catalyst for 30 min. (c) n.d. = not determined. (d) Determined by HPLC (Daicel Chiralpack AD column). (e) Reaction time: 100 min.



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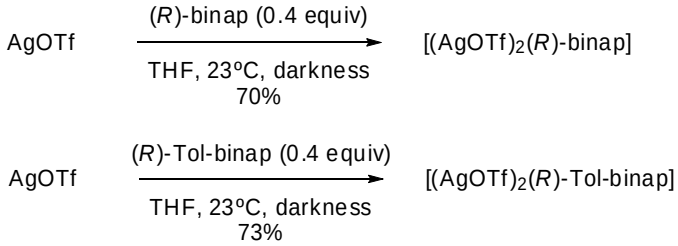
To achieve good levels of enantioselectivity it was important that the silver complexes did not contain residues of free AgOTf, as this salt can also catalyze the reaction and therefore the e.r. values could be decreased.



Scheme 54

The chromatogram of the enantiomerically enriched sample obtained in the reaction of (*E*)-**88** with [$(AgOTf)_2$(*R*).Tol-binap] at 50ºC (Table 3, entry 8) is shown in Figure 7. The absolute configuration of the major enantiomer was not determined.

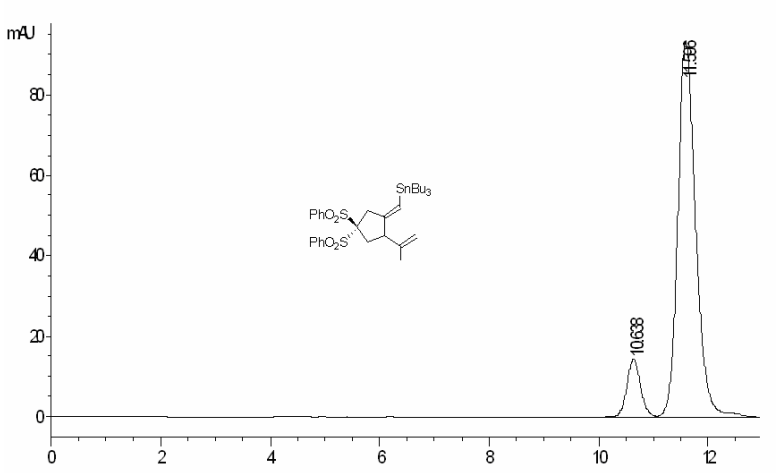
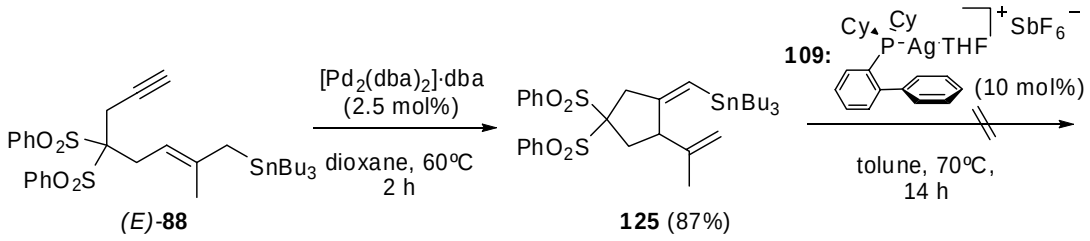


Figure 7. *ChiralPack AD* column (99:1 hexane-*i*-PrOH, flow = 0.7 mL/min; λ = 254 nm).

3. Mechanistic studies on the intramolecular carbostannylation of alkynes

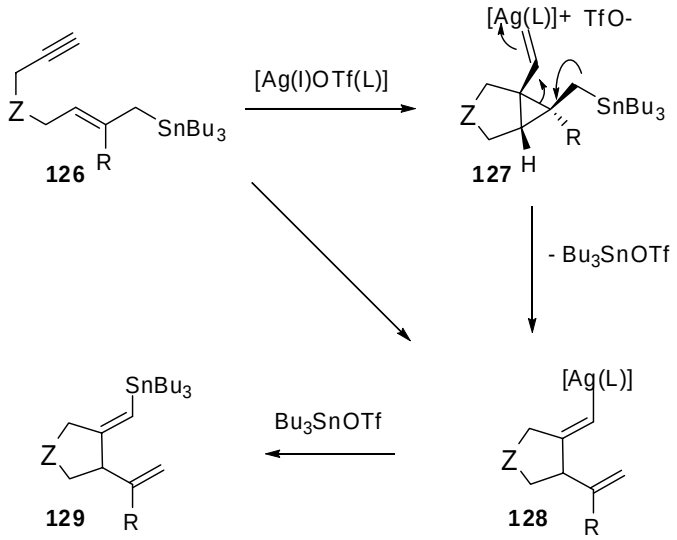
Yamamoto and co-workers have suggested that a transmetalation between the silver(I) complex and allyl trimethoxysilanes may take place.[9,10b] However, in the reactions of allylstannanes with aldehydes, the silver(I) complex was proposed to act as a chiral Lewis acid rather than forming an allyl-silver(I) species.[7] A transmetalation of the allylstannane with silver(I) followed by insertion of the allyl-silver(I) species into the alkyne would lead to alkenyl stannanes with a *Z* configuration at the double bond, as occurred in the catalysis with Pd(0).[42] Some experiments were carried out in order to gain more insight in the reaction mechanism. It is reasonable to think that if the *E* product is the most thermodynamically stable it could be formed from the *Z*-isomer by isomerization under the reaction conditions. To exclude this possibility, we prepared the *Z* isomer **125** by the cyclization of (*E*)-**88** with $[Pd_2(dba)_3]\cdot dba$ as the catalyst.[42] However, no isomerization of this substrate into **100** was observed after the substrate was heated with complex **109** in toluene at 70ºC for 14 h (Scheme 55).



Scheme 55

This result confirmed that the *E* isomer, which was the only isomer observed in all reactions, is the only isomer formed in the cyclization and that no isomerization takes place under the reaction conditions.

The formation of silver(I)-acetylide complexes is not a major pathway under these reaction conditions.[60] Instead, the isolation of alkenylstannanes of type **129** is consistent with a mechanism in which the silver(I) complex selectively activates the alkyne of **126** to form cyclopropyl carbene-silver(I) complex **127**, followed by cleavage of the cyclopropanes to form the alkenyl-silver(I) complex **128**.[43,61,62] Reaction of **128** with Bu_3SnOTf (or a similar electrophile in the case of $AgSbF_6$ or catalyst **109**) gives the stannanes **129**. Alternatively, formation of **128** might take place in a single step as shown in Scheme 56.



Scheme 56

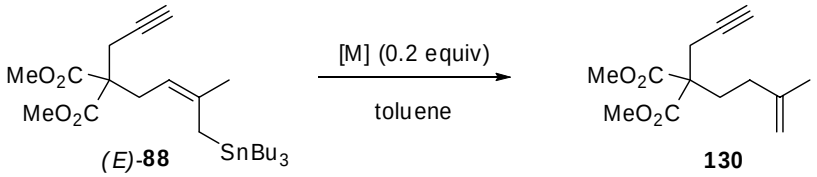
To investigate whether silver is acting as a simple Lewis acids or not, we tested the cyclization of (*Z*)-**82** with various Lewis acids that gave good yields in the

60 (a) Létinois-Halbes, U.; Pale, P.; Berger, S. *J. Org. Chem*. **2005**, *70*, 9185-9190. (b) Vitérisi, A.; Orsini, A.; Weibel, J.-M.; Pale, P. *Tetrahedron Lett*. **2006**, *47*, 2779-2781, and references therein.

61 Méndez, M.; Echavarren, A. M. *Eur. J. Org. Chem*. **2002**, 15-28.

62 (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2004**, *43*, 2402-2406. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J*. **2006**, *12*, 1677-1693. (c) Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Cárdenas, D. J.; Buñuel, E.; Nevado, C.; Echavarren, A. M. *Angew. Chem. Int. Ed*. **2005**, *44*, 6146-6148. (d) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Eur. J*. **2006**, *12*, 5916-5923.

intermolecular allylstannylation of alkynes developed by Yamamoto.[47] Treatment of (*Z*)-**88** with $ZrCl_4$ led only to partial destannylation of the starting material as shown in Scheme 57. The same occurred when (*Z*)-**88** was treated with $EtAlCl_2$ under similar reaction conditions. Application of our standard reaction conditions, heating in toluene at 70ºC, in the reaction of (*Z*)-**88** with $EtAlCl_2$ (0.2 equiv) led again to destannylated product **130**.



(E)-**88** **130**

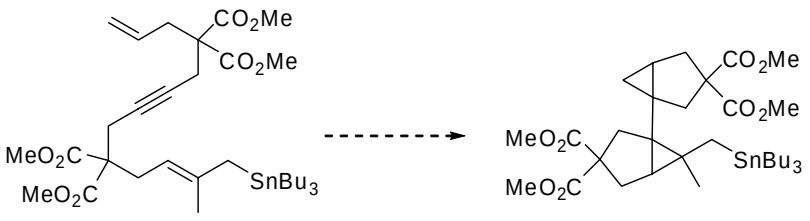
M = $ZrCl_4$, -78-0ºC, 24 h 33%

M = $EtAlCl_2$, -78-0ºC, 24 h 40%

Scheme 57

Attempts were made to trap the cyclopropyl carbene-silver(I) complex **127** by adding external olefins to the reaction of allylstannanes-alkynes (*Z*)- **88**,(*E*),-**88**, **89** with complex **109** or $[AgOTf(PPh_3)]_3$. Nonetheless, the addition of 5-10 equiv of 2-norbornone, cyclohexene, 1,3-cyclohexadiene, styrene, 2,5-dimetyl-hexa-2,4-diene, or 2,3-dihydrofurane led to the usual alkenylstannanes products (**100**, **101**) when reactions were performed at 70ºC. If the reactions were carried out at lower temperatures, the destannylated compounds (**102**, **124**) were obtained. Also the addition of external electrophiles such as benzaldehyde with the aim of trapping the alkenyl-silver(I) intermediate (**128**) led to the isolation of the destannylated compounds.

Intramolecular trapping of the carbene intermediate, would be more facile than the intermolecular reaction therefore, compound **131** was prepared. Trapping of the cyclopropyl carbene intermediate by a second olefin would lead to compound **132** (Scheme 58).

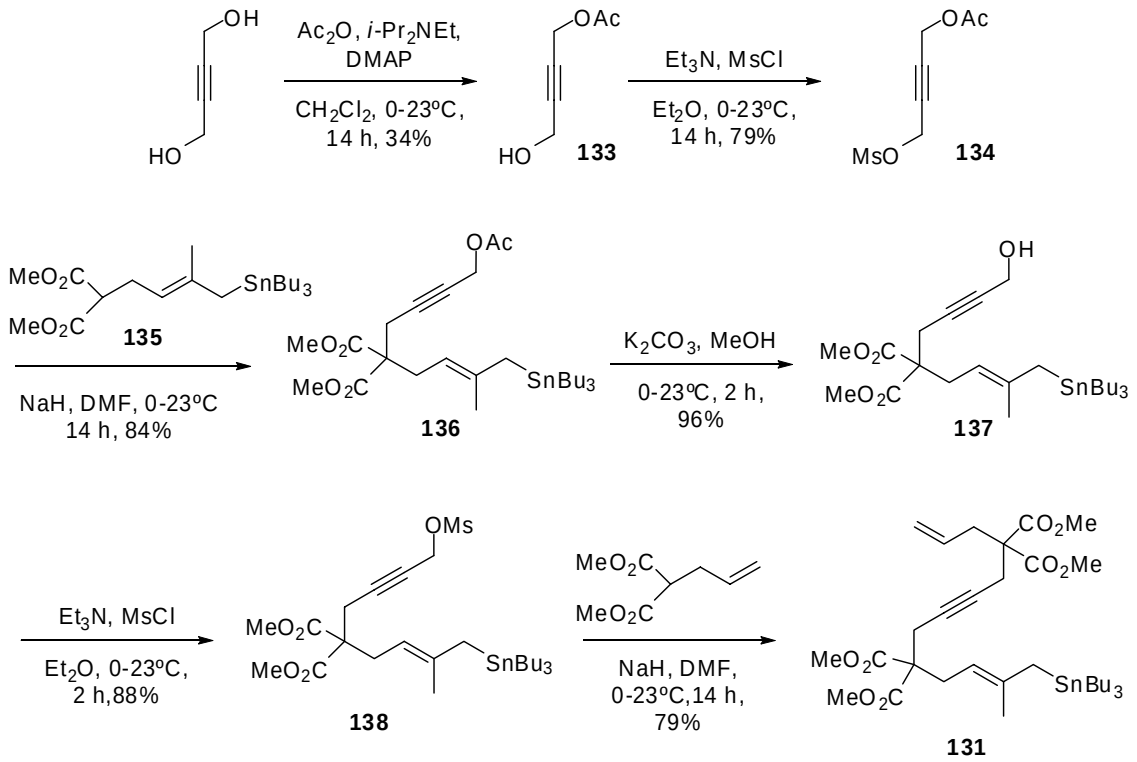


131 **132**

Scheme 58

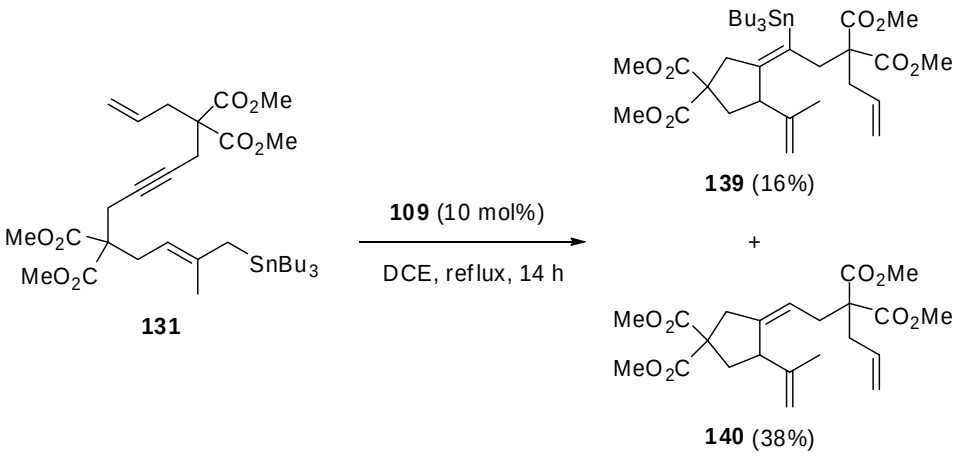
47 Matsukawa, Y.; Asao, N.; Kitahara, H.; Yamamoto, Y. *Tetrahedron Lett*. **1999**, *55*, 3779-3790.

The synthesis of compound **131** is depicted in Scheme 59. Starting from 2-butyne-1,4-diol, the monoacetate **133** was obtained in 34% yield by a standard acetylation procedure. Introduction of a mesylate at the second hydroxyl group afforded **134**. Alkylation of stannane **135** with **134** gave the stannane derivative **136** in 84% yield. Subsequent methanolysis of the acetate with K_2CO_3 afforded the alcohol **137** which was further transformed to **138** by treatment with methanesulfonyl chloride (MsCl) and triethylamine. Finally, reaction of **138** with the sodium enolate of dimethyl allylmalonate afforded **131** in 79% yield.



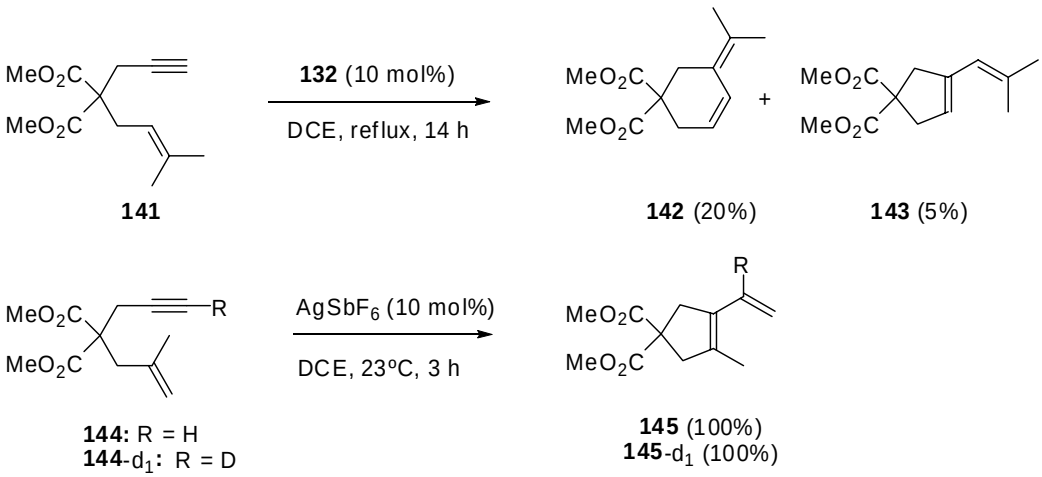
Scheme 59

The cyclization of **131** was examined with $[AgOTf(PPh_3)]_3$ and complex **109** in DCE. The first catalyst, led only to decomposition after heating at 80ºC for 2 days, whereas complex **109** led to stannane **139** in 16% yield and **140** in 38% yield (Scheme 60). These products arise from the usual carbostannylation of the alkyne with the allylstannane moiety. If the cyclopropyl carbene was formed, it immediately opened to give the alkenylstannane without trapping by the second olefin. Performing the reaction at lower temperatures resulted in extensive destannylation of **139**, and recovering of starting material.



Scheme 60

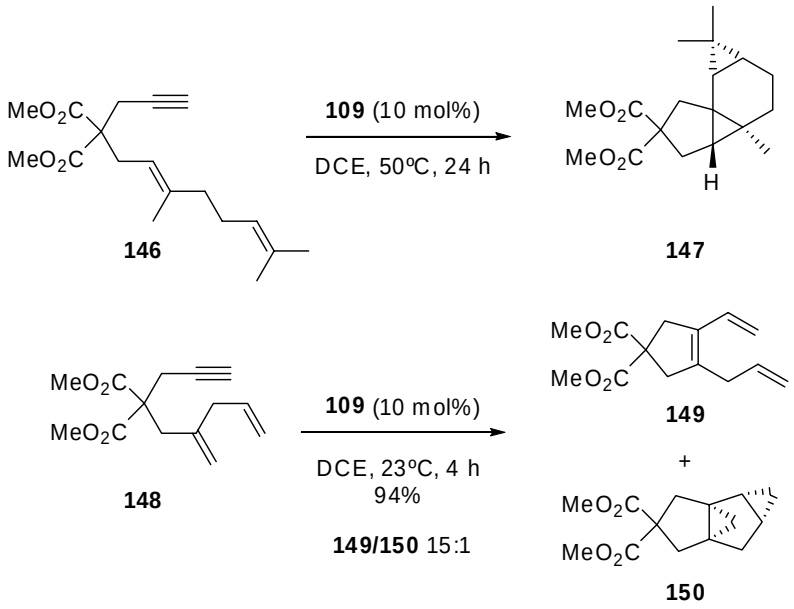
Since we were not successful in trapping the proposed cyclopropyl carbene intermediate (**127**) in the cyclization of allylstannes-alkynes, we decided to support the formation of silver carbenes in these reactions in an indirect way. Thus, reaction of simple enynes **141**, **144**, **146** and **148** with silver(I) catalysts was examined (Schemes 62 and 63). Initially, the cyclization of enyne **141** was tested. Under the best reaction conditions found for the cyclization of this substrate, compounds **142** and **143** were obtained in low yield (Scheme 62). Surprisingly, the cyclization of **144** took place smoothly with $AgSbF_6$ to afford diene **145** in quantitative yield. This is the product of single cleavage skeletal rearrangement, as shown in the reaction of deuterated **144**-d_1 to give **145**-d_1.[62c]



Scheme 62

The reaction of dienyne **146** catalyzed by **109** led to **147** in 66% yield, along with the skeletal-rearrangement products as minor compounds. Tetracycle **147** is identical to the product obtained before using gold(I) catalysts with the same substrate, and it is formed by trapping of the initial cyclopropyl carbene by the olefin.[62d] In

contrast, **148** gave rise to a 15:1 mixture of the skeletal-rearrangement derivative **149** and the product of an intramolecular cyclopropanation **150** (94% yield, Scheme 76).[63]



Scheme 63

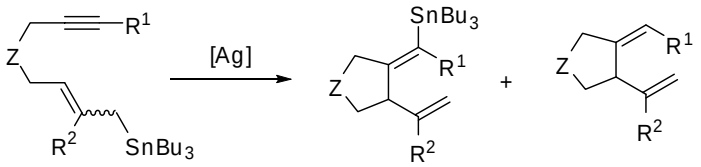
The results of Schemes 62 and 63 confirm that the proposed silver(I)-carbene species are the intermediates in the cyclization of simple enynes with silver salts or complexes. This suggests that silver(I)-carbenes are also involved in the intramolecular carbostannylation of alkynes

63 For closely related examples of intramolecular cyclopropanation reactions catalyzed by ruthenium(II) or platinum(II), see: Peppers, B. P.; Diver, S. T. *J. Am. Chem. Soc*. **2004**, *126*, 9524-9525.

Chapter 2. Conclusions

Conclusions

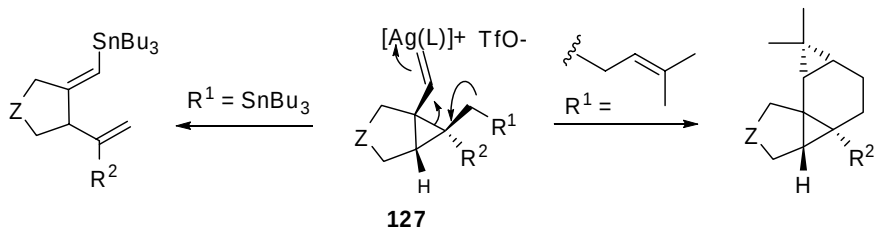
Silver(I) species catalyze the intramolecular carbostannylation of alkynes to give (*E*)-alkenylstannanes stereoselectively as single isomers. The reaction proceeds satisfactorily regardless the *E*/*Z* configuration at the allylstannane-alkynes derivatives (**152**). Together with the (*E*)-alkenylstannanes **152** small amounts of the destannylated products **153** were observed in some cases (Scheme 63). This methodology can be further applied for the preparation of six- and seven-membered rings.



151 **152** **153**

Scheme 63

Enantiomeric excesses of 78% can be achieved by performing the cyclization with [$(AgOTf)_2$(*R*)-Tol-binap] as catalyst. The reaction mechanism appears to be mechanistically similar to that of the reaction of enynes with other electrophilic transition-metal complexes. In this case, the cyclopropyl silver(I)-carbene **127**, opens to give an alkenyl-silver intermediate, which can react with the tin electrophile generated *in situ*, thus leading to stannanes with total control of the stereoselectivity (Scheme 64). The participation of cyclopropyl silver(I)-carbenes in these transformations was supported by the fact that 1,6-enynes were found to undergo cyclizations with silver(I) to afford products of skeletal rearrangements and intramolecular cyclopropanation.



127

Scheme 64

Chapter 2. Experimental Section

Experimental section: Index

Methods and Materials:

400 MHz ^{1}HMR, 100 MHz ^{13}C NMR, and 162 MHz ^{31}P NMR spectra were recorded at 23 ºC on a Bruker Avance 400 Ultrashield. Mass Spectrometry was performed on Waters LCT Premier (ESI) and Waters GCT (EI, CI) spectrometers. Infrared spectra were recorded on a Bruker Tensor 27 equipped with MKII Golden Gate Specac Single reflection ATR system. Melting points were determined using a Büchi-B450 apparatus. Thin layer chromatography was carried out using TCL-Aluminium sheets with 0.2 mm of silica gel (Merk GF_{234}). Column chromatography purifications were performed using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 μm). For the purifications of the stannane derivatives, the silica was first deactivated with triethylamine (5%). Analytical high-performance liquid chromatography (HPLC) was done with a chiral column (4.6 mm x 25 cm, Daicel Chiralpack AD). Optical rotation was measured on a P-1030 polarimeter from Jasco at the sodium D line.

All reactions and manipulations were performed under Ar or N_2 in standard laboratory glassware. Silver complexes were stored under Ar and protected from light. Solvents were dried using a Solvent Purification System (SPS). Extractive workup refers to partitioning of the crude reaction between an organic solvent and water, phase separation, drying (Na_2SO_4 or $MgSO_4$), and evaporation under reduced pressure. The saturated aqueous NH_4Cl solution was adjusted to pH = 8 by addition of NH_4OH.

Catalysts:

Silver salts: $AgBF_4$, AgO_2CCF_3, AgOTf, $AgSbF_6$, were purchased from Aldrich and weighted in a glove box. Complexes $[Pd_2(dba)_3]\cdot dba$,[64] $[Pd(PPh_3)_3]$[65] and $[Au\{P[C_6H_4(o\text{-}Ph)](tBu)_2\}(NCMe)]SbF_6$[57] were prepared according to described procedures.

$[AgOTf(PPh_3)_3]$[52]

To a of AgOTf (100 mg, 0.39 mmol) in Et_2O solution (5 mL) was added a solution of PPh_3 (99 mg, 0.38 mmol) in Et_2O (5mL). A white solide appeared an the

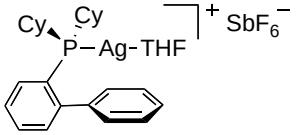
64 Takahashi, Y.; Ito, Ts.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun*. **1970**, *17*, 1065-1066.

65 Cotton, F. A. *Inorg. Synth*. **1972**, *13*, 121.

52 Bajardí, M.; Crespo, O.; Laguna, A.; Fishcer, K. *Inorg. Chim. Acta* **2000**, 304-7-16.

mixture was stirred for about 1 h protected from light. The solid was filtered off, washed with Et_2O and dried. Obtained: 121 mg, 60%.

Synthesis of silver complex 109.



To a suspension of $AgSbF_6$ (104 mg, 305 mmol) in THF (5 mL) was added 2-biphenyldicyclohexylphosphine (107 mg, 305 mmol) dissolved in THF (5 mL). The reaction mixture was stirred for 2 h in the dark, then the solvent was reduced to 3 mL and the solution was filtered through a pad of Celite. Addition of Et_2O (2 mL) afforded the product as a white crystalline solid which was filtered off and washed with pentane to give **109** (175 mg, 75%): mp 174-176ºC: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.67-7.51 (m, 6H), 7.38-7.33 (m, 1H), 7.30-7.24 (m, 2H), 3.84-3.71 (m, 4H), 2.25-2.07 (m, 2H), 1.94-1.75 (m, 9H), 1.75-1.66 (m, 2H), 1.66-1.57 (m, 2H), 1.42-1.09 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.20 (d, $J(^{13}C\text{-}^{31}P)$ = 17.5 Hz), 141.20 (d, $J(^{13}C\text{-}^{31}P)$ = 8.9 Hz), 132.46, 131.42 (d, $J(^{13}C\text{-}^{31}P)$ = 6.6 Hz), 130.7 (d, $J(^{13}C\text{-}^{31}P)$ = 1.8 Hz), 129.19, 128.77, 128.33, 128.08 (d, $J(^{13}C\text{-}^{31}P)$ = 4.9 Hz), 124.96 (d, $J(^{13}C\text{-}^{31}P)$ = 34.9 Hz), 69.02, 34.68 (d, $J(^{13}C\text{-}^{31}P)$ = 19.6 Hz), 31.10 (d, $J(^{13}C\text{-}^{31}P)$ = 9.3 Hz), 29.18, 26.64 (d, $J(^{13}C\text{-}^{31}P)$ = 9.3 Hz), 26.54 (d, $J(^{13}C\text{-}^{31}P)$ = 12.9 Hz), 25.51 (d, $J(^{13}C\text{-}^{31}P)$ = 3.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.31 (d, $J(^{31}P\text{-}^{109}Ag)$ = 844.18, $J(^{31}P\text{-}^{107}Ag)$ = 733.21 Hz). HRMS-ESI Calcd for $C_{24}H_{31}PAg$ $[M\text{-}C_4H_8SbF_6]^+$: 457.1214. Found: 457.1213.

Chiral Catalysts.[10b]

Chiral complexes $[(AgSbF_6)_2(R)$-Tol-binap], $[(AgOTf)_2(R)$-binap] and $[(AgOTf)_2(R)$-Tol-binap], were synthesized as follows: To a solution of the silver salt (0.54 mmol) in THF (7 mL), was added the chiral phosphine (0.22 mmol) dissolved in THF (7 mL). The mixture was stirred protected from light at 23ºC for 2 h, the solvent was reduced to 5 mL in vacuo and the solution was filtered through a pad of Celite. Removing of the solvent under vacuum afforded the complexes as white solids in 70-73% yield.

10b Momiyama, N.; Yamamoto, H. *J. Am. Chem Soc*. **2004**, *126*, 5360-5361.

[$(AgSbF_6)_2$(*R*)-Tol-binap]: ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.86 (d, $J(^{31}P\text{-}^{109}Ag)$ = 869.71, $J(^{31}P\text{-}^{107}Ag)$ = 749.50 Hz).

[$(AgOTf)_2$(*R*)-binap]: ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.82 (d, $J(^{31}P\text{-}^{109}Ag)$ = 854.09, $J(^{31}P\text{-}^{107}Ag)$ = 741.14 Hz).

[$(AgOTf)_2$(*R*)-Tol-binap]: ^{31}P NMR (162 MHz, $CDCl_3$) δ 5.55 (d, $J(^{31}P\text{-}^{109}Ag)$ = 858.66, $J(^{31}P\text{-}^{107}Ag)$ = 744.63 Hz).

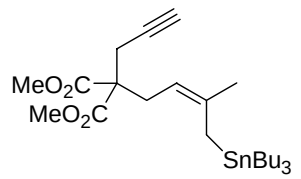
General procedure for alkylation with NaH

To a suspension of NaH (60% in mineral oil, 1.60 mmol) in DMF (10 mL) at 0ºC was added a solution of substrate (1.60 mmol) in DMF (5 mL). The mixture was stirred for 10 min, after which the alkynyl halide (1.60 mmol) was added. The reaction mixture was stirred at 23ºC for 16 h. After extractive work-up (Et_2O/water/brine) and chromatography (hexane-EtOAc) the title compounds were obtained.

Synthesis of Allylstannanes (*Z*)-82, (*E*)-82, 87, (*Z*)-88, (*E*)-88, 89 and 94

These substrates were prepared by propargylation with propargyl bromide of the following stannanes: dimetyl 2-[(*E*)-3-methyl-4-tributylstannyl-2-butenyl]malonate, dimetyl 2-[(*Z*)-3-methyl-4-tributylstannyl-2-butenyl]malonate, dimethyl 2-[(*E*)-4-tributylstannyl-2-butenyl]malonate, (*Z*)-5,5-bis(phenylslfonyl)-2-penten-yl-1-tri-*n*-butylstannane, (*E*)-5,5-bis(phenylsulfonyl)-3-methyl-2-penten-1-yl-tri-*n*-butylstannane, and (Z)-5,5-bis(phenylsulfonyl)-3-methyl-2-penten-1-yl-tri-*n*-butylstannane, and 6,6-biis(phenylsulfonyl)-3-methyl-1-(tri-*n*-butylstannyl)-2-hexene. The synthesis of theses substrates was described in Chapter 1.

Dimethyl 2-((*Z*)-3-Methyl-4-tri-*n*-butylstannyl-2-butenyl)-2-(propynyl)malonate ((*Z*)-82).[46]

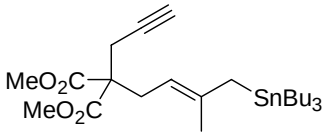


Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.59 (t, *J* = 7.5 Hz, 1H), 3.75 (s, 6H), 2.81 (d, *J* = 2.6 Hz, 2H), 2.73 (d, *J* = 7.2 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.79 (s,

46 Described as a mixture of *E*/*Z* isomers in: Miura, K.; Fujisawa, N.; Hosomi, A. *J. Org. Chem*. **2004**, *69*, 2427-2430.

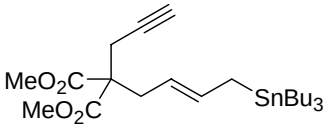
2H), 1.67 (br s, 3H), 1.55-1.46 (m, 6H), 1.39-1.27 (m, 6H), 0.98-0.79 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.57, 140.86, 111.66, 79.63, 71.05, 57.32, 52.63, 30.93, 29.11 ($^3J(^{119}$Sn-C) = 19 Hz), 27.38 ($^2J(^{119}$Sn-C) = 53 Hz), 26.34, 22.60, 15.61, 13.68, 9.75 ($^1J(^{119}$Sn-C) = 314, (^{117}Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{25}H_{44}O_4Na^{120}Sn$ $[M+Na]^+$: 551.2159. Found: 551.2183.

Dimethyl 2-((*E*)-3-Methyl-4-tri-*n*-butylstannyl-2-butenyl)-2-(propynyl)malonate ((*E*)-82).[46]



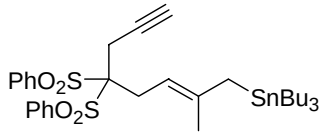
Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.71 (t, *J* = 7.5 Hz, 1H), 3.75 (s, 6H), 2.84-2.75 (m, 4H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.75 (s, 2H), 1.65 (s, 3H), 1.55-1.41 (m, 6H), 1.37-1.22 (m, 6H), 0.98-0.71 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 170.56 (C), 140.56 (C), 112.03 (CH), 71.06 (CH_2), 57.29 (C), 52.65 (CH_3), 31.03 (CH_2), 29.15 ($^3J(^{119}$Sn-C) = 20 Hz, CH_2), 27.37 ($^2J(^{119}$Sn-C) = 53 Hz, CH_2), 22.64 (CH_2), 22.44 (CH_2), 18.78 (CH_3), 13.70 (CH_3), 9.43 ($^1J(^{119}$Sn-C) = 312, (^{117}Sn-C) = 299 Hz, CH_2). HRMS-ESI Calcd for $C_{25}H_{44}O_4Na^{120}Sn$ $[M+Na]^+$: 551.2159. Found: 551.2147.

Dimethyl 2-((*E*)-4-Tri-*n*-butylstannyl-2-butenyl)-2-(propynyl)malonate (87).[43]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.81-5.61 (m, 1H), 5.01-4.89 (m, 1H), 3.73 (s, 6H), 2.77 (d, *J* = 2.6 Hz, 2H), 2.73 (d, *J* = 7.4 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.69 (d, *J* = 8.8 Hz, 2H), 1.56-1.42 (m, 6H), 1.36-1.24 (m, 6H), 0.96-0.74 (m, 15H).

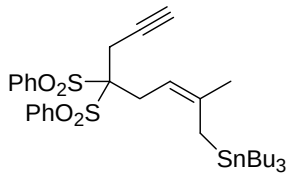
(*E*)-4,4-Bis(phenylsulfonyl)-8-tri-*n*-butylstannyl-7-methyl -6-octen-1-yne ((*E*)-88).



43 (a) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc*. **2000**, *122*, 1221-1222. (b) Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem*. **2002**, *123*, 8416-8417.

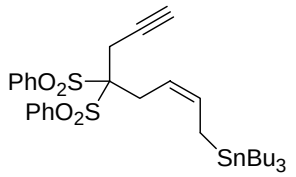
Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.20-8.11 (m, 4H), 7.75-7.68 (m, 2H), 7.63-7.55 (m, 4H), 5.27 (br t, J = 6.4 Hz, 1H), 3.17 (d, J = 2.6 Hz, 2H), 3.05 (d, J = 6.5 Hz 2H), 2.10 (t, J = 2.5 Hz, 1H), 1.83 (s, 2H), 1.58 (s, 3H), 1.55-1.42 (m, 6H), 1.37-1.26 (m, 6H), 0.99-0.80 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.68, 136.62, 134.57, 131.57, 128.45, 109.58, 89.69, 76.38, 73.89, 29.07 ($^{3}J(^{119}$Sn-C) = 19 Hz), 27.87, 27.40 ($^{2}J(^{119}$Sn-C) = 53 Hz), 22.89, 20.28, 13.72, 9.60 ($^{1}J(^{119}$Sn-C) = 314, $^{1}J(^{117}$Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{33}H_{48}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 715.1914. Found: 715.1934.

(*Z*)-4,4-Bis(phenylsulfonyl)-8-tri-*n*-butylstannyl-7-methyl-6-octen-1-yne ((*Z*)-88).



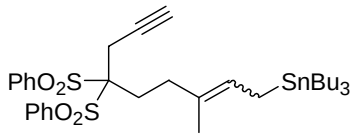
Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.19-8.10 (m, 4H), 7.75-7.67 (m, 2H), 7.63-7.53 (m, 4H), 5.09 (br t, J = 6.1 Hz, 1H), 3.21 (d, J = 2.9 Hz, 2H), 3.01-2.91 (m, 2H), 2.08 (t, J = 2.7 Hz, 1H), 1.77-1.22 (m, 17H), 0.99-0.73 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.07, 136.79, 134.54, 131.59, 128.41, 109.43, 89.08, 76.29, 73.85, 29.07 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.36 ($^{2}J(^{119}$Sn-C) = 57 Hz), 20.64, 17.53, 16.01, 13.69, 13.60, 9.90 ($^{1}J(^{119}$Sn-C) = 314, $^{1}J(^{117}$Sn-C) = 303 Hz). HRMS-ESI Calcd for $C_{33}H_{48}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 715.1914. Found: 715.1938.

(*Z*)-4,4-Bis(phenylsulfonyl)-8-tri-*n*-butylstannyl-6-octen-1-yne (89).



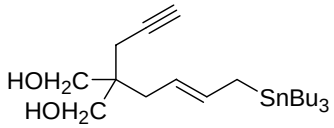
Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.20-8.12 (m, 4H), 7.76-7.69 (m, 2H), 7.64-7.54 (m, 4H), 5.93-5.79 (m, 1H), 5.47-5.34 (m, 1H), 3.23 (d, J = 2.8 Hz, 2H), 3.08-2.98 (m, 2H), 2.09 (t, J = 2.7 Hz, 1H), 1.70 (d, J = 9.4 Hz, 2H), 1.57-1.41 (m, 6H), 1.37-1.24 (m, 6H), 0.98-0.72 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.56, 134.62, 133.82, 131.59, 128.49, 113.72, 89.26, 76.16, 73.95, 29.12 ($^{3}J(^{119}$Sn-C) = 21 Hz), 27.33 ($^{2}J(^{119}$Sn-C) = 53 Hz), 26.76, 20.42, 13.70, 11.30, 9.60 ($^{1}J(^{119}$Sn-C) = 318, $^{1}J(^{117}$Sn-C) = 303 Hz). HRMS-ESI Calcd for $C_{32}H_{46}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 701.1757. Found: 701.1764.

4,4-Bis(phenylsulfonyl)-9-tri-*n*-butylstannyl-7-methyl-7-nonen-1-yne (94).[43]



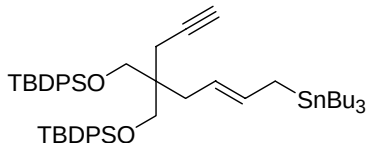
5:1 *E*/*Z* mixture of isomers: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.17-8.09 (m, 4H), 7.77-7.69 (m, 2H), 7.64-7.55 (m, 4H), 5.41 (t, *J* = 8.9 Hz, 1H, *E*), 5.36 (m, 1H, *Z*), 3.30 (d, *J* = 2.7 Hz, 2H, *Z*), 3.26 (d, *J* = 2.7 Hz, 2H, *E*), 2.54-2.32 (m, 4H), 2.07 (t, *J* = 2.7 Hz, 1H, Z), 2.05 (t, *J* = 2.7 Hz, 1H, *E*), 1.74 (d, *J* = 9.1 Hz, 2H, Z), 1.66 (d, *J* = 9.0 Hz, 2H, E), 1.57 (br s, 3H), 1.54-1.44 (m, 6H), 1.37-1.25 (m, 6H), 0.97-0.74 (m, 15H).

2-((*E*)-4-Tri-*n*-butylstannyl-2-butenyl)-2-(2-propynyl)-1,3-propanediol (90).



To a suspension of $LiAlH_4$ (37 mg, 0.97 mmol) in Et_2O (10 mL) at 0ºC was slowly added a solution of **87** (356 mg, 0.69 mmol) in Et_2O (5 mL). The reaction was stirred from 0ºC to 23ºC for 3 h and was subsequently cooled to 0ºC and quenched by addition of a saturated solution of NH_4Cl. After usual extractive work-up (Et_2O/water) and purification by column chromatography (2:1 hexane-EtOAc) the product was obtained as a colorless oil (238 mg, 75%). Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.75-5.61 (m, 1H), 5.26-5.15 (m, 1H), 3.72-3.61 (m, 4H), 2.27 (d, *J* = 2.41 Hz, 2H), 2.21-2.12 (br s, 2H), 2.07 (d, *J* = 7.3 Hz, 2H), 2.03 (t, *J* = 2.6 Hz, 1H), 1.73 (d, *J* = 8.3 Hz, 2H), 1.60-1.42 (m, 6H), 1.38-1.26 (m, 6H), 0.97-0.78 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.97, 119.06, 81.21, 70.66, 67.82, 42.39, 35.10, 29.14 ($^3J(^{119}$Sn-C) = 20 Hz), 27.3 ($^2J(^{119}$Sn-C) = 53 Hz), 21.48, 14.49, 13.71, 9.19 ($^1J(^{119}$Sn-C) = 316, $^1J(^{117}$Sn-C) = 302 Hz). HRMS-ESI Calcd for $C_{22}H_{42}O_4Na^{120}Sn$ $[M+Na]^+$: 481.2104. Found: 481.2103.

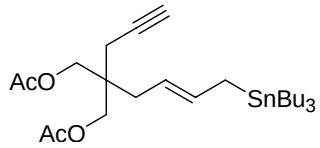
1,3-Bis(*tert*-butyl-diphenylsilyloxy)-2-((*E*)-4-tri-*n*-butylstannyl-2-butenyl)-2-(2-propynyl)propane (91).



To a solution of **90** (130 mg, 0.29 mmol) and imidazole (140 mg, 2.06 mmol) in DMF (10 mL) at 0ºC was added TBDPSCl (0.45 mL, 1.76 mmol). The reaction mixture

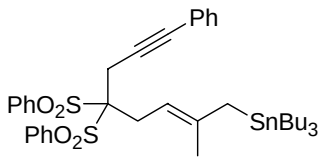
was stirred at 23ºC overnight. After extractive workup (Et_2O/H_2O) and chromatography (10:1 hexane-EtOAc), **91** was obtained as a colorless oil, (200 mg, 98%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.80-7.61 (m, 8H), 7.50-7.30 (m, 12H), 5.56 (m, 1H), 4.97 (m, 1H), 3.63, 3.60 (AB system, J_{AB} = 9.6 Hz, 4H), 2.26 (d, J = 2.5 Hz, 2H) 2.14 (d, J = 7.5 Hz, 2H), 1.85 (t, J = 2.4 Hz, 1H), 1.60 (d, J = 8.3 Hz, 2H), 1.53-1.40 (m, 6H), 1.37-1.23 (m, 6H), 1.08 (s, 18H), 0.96-0.73 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.84, 133.61, 133.59, 132.85, 129.51, 129.50, 127.56, 127.53, 119.88, 81.88, 70.10, 64.75, 44.44, 34.08, 29.15 (^3J(^{119}Sn-C) = 20 Hz), 27.34, 26.98, 21.43, 19.40, 14.43, 13.76, 9.13 (^1J(^{119}Sn-C) = 314, ^1J(^{117}Sn-C) = 300 Hz). Anal. Calcd for $C_{54}H_{78}O_2SnSi_2$: C, 69.44; H, 8.42. Found: C, 69.78; H, 8.18. HRMS-ESI Calcd for $C_{54}H_{78}O_2Na^{120}SnSi_2$ $[M+Na]^+$: 957.4460. Found: 957.4480.

1,3-Diacetoxy-2-((*E*)-4-tri-*n*-butylstannyl-2-butenyl)-2-(3-propynyl)propane (92).



To a solution of **90** (180 mg, 0.39 mmol) and DMAP (24 mg, 0.50 mmol) in CH_2Cl_2 (10 mL) at 0ºC was added *i*-$PrEt_2N$ (0.29 mL, 1.70 mmol) and Ac_2O (0.11 mL, 1.58 mmol). The resulting mixture was stirred at 23ºC overnight. After extractive workup (CH_2Cl_2/H_2O) and chromatography (6:1 hexane-EtOAc), **115** was obtained as a colorless oil (198 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73-5.61 (m, 1H), 5.20-5.07 (m, 1H), 4.08-3.96 (m, 4H), 2.24 (d, J = 2.6 Hz, 2H), 2.15, (d, J = 7.3 Hz, 2H), 2.08 (s, 6H), 2.02 (t, J = 2.7 Hz, 1H), 1.73 (d, J = 8.7 Hz, 2H), 1.59-1.40 (m, 6H), 1.37-1.25 (m, 6H), 0.98-0.78 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.74, 134.97, 117.72, 79.64, 71.08, 65.52, 40.28, 34.59, 29.12 (^3J(^{119}Sn-C) = 20 Hz), 27.32 (^2J(^{119}Sn-C) = 52 Hz), 21.94, 20.82, 14.59, 13.70, 9.18 (^1J(^{119}Sn-C) = 316, (^{117}Sn-C) = 303 Hz). HRMS-ESI Calcd for $C_{26}H_{46}O_4Na^{120}Sn$ $[M+Na]^+$: 565.2316. Found: 565.2330.

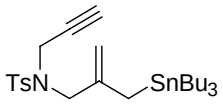
(*E*)-4,4-Bis(phenylsulfonyl)-8-tri-*n*-butylstannyl-7-methyl-6-octen-1-phenyl-1-yne (93).



To a suspension of NaH (60% in mineral oil, 24 mg, 0.61 mmol) in DMF (10 mL) was added (*E*)-5,5-bis(phenylsulfonyl)-3-methyl-2-penten-1-yl-tri-*n*-butylstannane

(400 mg, 0.61 mmol) in DMF (3 mL) at 0ºC. The mixture was stirred for 15 min, after which (3-bromo-1-propynyl)benzene (140 mg, 0.73 mmol) in DMF (3 mL) was added. The reaction was stirred overnight at 23ºC, and was subjected to the usual extractive workup (Et_2O/H_2O). The crude was purified by column chromatography (10:1 to 8:1 hexane-EtOAc) to yield **93** as a vitreous solid, (350 mg, 75%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.24-8.14 (m, 4H), 7.72-7.64 (m, 2H), 7.60-7.52 (m, 4H), 7.39-7.25 (m, 5H), 5.34 (t, *J* = 6.6 Hz, 1H), 3.38 (s, 2H), 3.11 (d, *J* = 6.6 Hz, 2H), 1.84 (s, 2H), 1.57 (s, 3H), 1.53-1.39 (m, 6H), 1.35-1.23 (m, 6H), 0.98-0.76 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.93, 136.96, 134.45, 131.60, 131.56, 128.43, 128.25, 128.18, 122.91 109.74, 90.15, 85.77, 82.25, 29.13 ($^3J(^{119}$Sn-C) = 20 Hz), 28.16, 27.37 ($^2J(^{119}$Sn-C) = 55 Hz), 22.93, 21.31, 19.14, 13.72, 9.55 ($^1J(^{119}$Sn-C) = 314, $^1J(^{117}$Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{39}H_{52}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 791.2227. Found: 791.2247.

_N_-[(2-Methyltri-_n_-butylstannyl)-2-propenyl]-_N_-porpargyl-4-(toluene)sulfonamide (95).

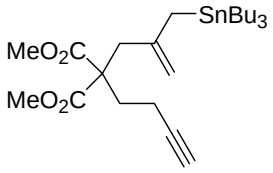


To a suspension of NaH (60% in mineral oil, 100 mg, 2.63 mmol) in DMF (15 mL) was added *N*-2-propynyl-(4-toluene)-sulfonamide[53] (540 mg, 2.63 mmol) in DMF (5 mL) at 0ºC. The mixture was stirred for 15 min after which 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene[54] (1 g, 2.63 mmol) in DMF (5mL) was added at 0ºC. The reaction was stirred overnight at 23ºC and was subjected to the usual extractive workup (Et_2O/H_2O). The crude mixture was purified by column chromatography (20:1 hexane-EtOAc) to yield **95** as a colorless oil, (780 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.74 (s, $^4J(^{119}$Sn-H) = 17.6 Hz, 2H), 4.10 (d, , *J* = 2.3 Hz, 1H), 3.64 (s, 2H), 2.44 (s, 3H), 1.96 (t, *J* = 2.3 Hz, 1H), 1.81 (s, 2H), 1.57-1.43 (m, 6H), 1.39-1.27 (m, 6H), 1.0-0.82 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.38, 143.32, 136.17, 129.36, 127.85, 109.75, 76.62, 73.64, 52.50, 35.51, 27.38 ($^3J(^{119}$Sn-C) = 20 Hz), 21.54 ($^2J(^{119}$Sn-C) = 55 Hz), 15.21, 13.70, 9.49 ($^1J(^{119}$Sn-C) = 319, (^{117}Sn-C) = 304 Hz). HRMS-ESI Calcd for $C_{26}H_{43}NO_2NaS^{120}Sn$ $[M+Na]^+$: 576.1934. Found: 576.1957.

53 Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C. Y. *Tetrahedron Lett*. **1988**, *29*, 6433-6436.

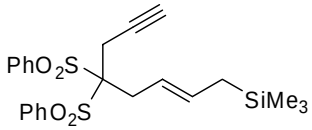
54 Keck, G. E.; Yu, T.; McLaws, M. D. *J. Org. Chem*. **2005**, *70*, 2543-2550.

Dimethyl 2-(2-Methyltri-*n*-butylstannyl-2-propenyl)-2-(4-but-1-ynyl)malonate (97).



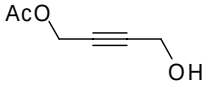
To a suspension of NaH (60% in mineral oil, 100 mg, 2.63 mmol) in DMF (15 mL) was added dimethyl 2-(3-butynyl)malonate[55] (480 mg, 2.63 mmol) in DMF (5 mL) at 0ºC. The mixture was stirred for 15 min after which 2-(chloromethyl)-3-(tri-*n*-butylstannyl)propene (1 g, 2.63 mmol) in DMF (5mL) was added at 0ºC. The reaction was stirred overnight at 23ºC and was subjected to the usual extractive workup (Et_2O/H_2O). The crude mixture was purified by column chromatography (40:1 to 20:1 hexane-EtOAc) to yield **97** as a colorless oil, (480 mg, 35%).^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (s, $^4J(^{119}$Sn-H) = 19.4 Hz, 1H), 4.46 (s, $^4J(^{119}$Sn-H) = 18.0 Hz, 1H), 3.73 (s, 6H), 2.62 (s, 2H), 2.24 (m, 2H), 2.18 (m, 2H), 1.96 (t, *J* = 2.4 Hz, 1H), 1.65 (s, ^2J(Sn-H) = 60.4 Hz, 2H), 1.56-1.40 (m, 6H), 1.38-1.25 (m, 6H), 1.0-0.79 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171. 48, 144.24, 109.73, 83.25, 68.59, 56.80, 52.40, 40.49, 31.67, 29.06 ($^3J(^{119}$Sn-C) = 19 Hz), 27.34 ($^2J(^{119}$Sn-C) = 54 Hz), 19.84 ($^1J(^{119}$Sn-C) = 234, (^{117}Sn-C) = 225 Hz), 14.17, 13.68, 9.47 ($^1J(^{119}$Sn-C) = 318, (^{117}Sn-C) = 304 Hz). HRMS-ESI Calcd for $C_{25}H_{44}O_4Na^{120}Sn$ $[M+Na]^+$: 551.2159. Found: 551.2146.

(*E*)-4,4-Bis(phenylsulfonyl)-8-trimethylsilyl-6-octen-1yne (122).[43b]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.19-8.12 (m, 4H), 7.77-7.69 (m, 2H), 7.65-7.56 (m, 4H), 5.75 (dt, *J* = 16.4, 8.2, 1.1 Hz, 1H), 5.49 (dt, *J* = 14.9, 7.0, 1.1 Hz, 1H), 3.17 (d, *J* = 2.6 Hz, 2H), 3.07 (d, *J* = 7.0 Hz, 2H), 2.11 (t, *J* = 2.6 Hz, 1H), 0.0 (s, 6H).

4-Hydroxy-2-butynyl Acetate (133).[66]

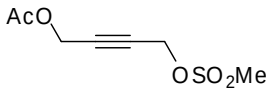


55 Casey, C. P.; Dzwiniel, T. L.; Kraft, S.; Guzei, I. A. *Organometallics* **2003**, *22*, 3915-3920.

66 Thorimbert, S.; Giambastiani, G.; Commandeur, C.; Vitale, M.; Poli, G.; Malacria, M. *Eur. J. Org. Chem*. **2003**, 2702-2708.

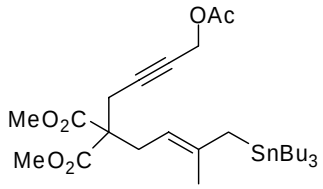
To a solution of 2-butyne-1,4-diol (5 g, 58 mmol), DMAP (1.4 g, 11.6 mmol) and *i*-Pr_2NEt (10.10 mL, 58 mmol) in CH_2Cl_2 (50 mL) was added Ac_2O (4.4 mL, 64 mmol) at 0ºC. The mixture was stirred at 23°C 14 h. After extractive workup (CH_2Cl_2/H_2O) and column chromatography (1:1 hexane-EtOAc) **133** was obtained as a colorless oil (2.5 g, 34%).^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.54 (s, 2H), 4.23 (s, 2H), 3.46-3.07 (br s, 1H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.65, 85.23, 79.17, 52.34, 50.57, 20.64.

4-(Methanesulfonyl)-2-butynyl Acetate (134).



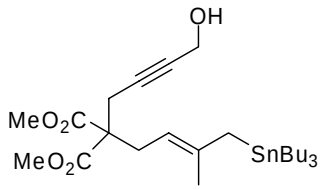
To a solution of **134** (2.5 g, 16.52 mmol) in diethtyl ether (60 mL) at 0ºC was slowly added methanesulfonyl chloride (1.3 mL, 29.28 mmol). The mixture was stirred at 23ºC for 14 h. After usual extractive workup (Et_2O/H_2O/brine) and column chromatography (3:1 to 1:1 hexane-EtOAc) **134** was obtained as a colorless oil (3.16g, 79%). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.87 (s, 2H), 4.72 (s, 2H), 3.11 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.08, 83.97, 78.70, 57.38, 51.70, 38.94, 20.58. HRMS-ESI Calcd for $C_7H_{10}O_5SNa$ $[M+Na]^+$: 229.0147. Found: 229.0137.

Dimethyl 2-(4-Acetoxy-2-butynyl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (136).



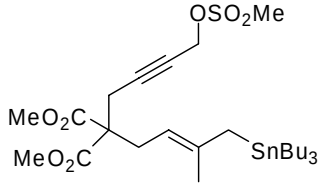
This compound was prepared from dimetyl 2-[(*E*)-3-methyl-4-tributylstannyl-2-butenyl]malonate and **134** following the general procedure for alkylation. After purification by column chromatography (10:1 to 4:1 hexane-EtOAc) the title compound was obtained as a colorless oil (84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.69 (t, J = 7.6 Hz, 1H), 4.63 (t, J = 2.0 Hz, 2H), 3.74 (s, 6H), 2.82 (t, J = 2.0 Hz, 2H), 2.76 (d, J = 7.9 Hz, 2H), 2.08 (s, 3H), 1.74 (s, 2H), 1.63 (s, 3H), 1.56-1.40 (m, 6H), 1.37-1.25 (m, 6H), 0.96-0.79 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.53, 170.18, 140.93, 112.07, 82.40, 76.84, 57.32, 52.65, 52.45, 31.13, 29.12 (^3J(^{119}Sn-C) = 20 Hz), 27.37 (^2J(^{119}Sn-C) = 54 Hz), 22.74, 22.62, 20.70, 18.71, 13.69, 9.44 (^1J(^{119}Sn-C) = 313, (^{117}Sn-C) = 299 Hz). HRMS-ESI Calcd for $C_{28}H_{48}O_6Na^{120}Sn$ $[M+Na]^+$: 623.2371. Found: 623.2349.

Dimethyl 2-(4-Hidroxy-2-butynyl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (137).



To a suspension of potassium carbonate (120 mg, 0.84 mmol) in MeOH (10 mL) was added **136** (420 mg, 0.70 mmol) dissolved in MeOH (5 mL). The mixture was stirred at 23ºC for 2h, after which a 0.2 M solution of HCl was added until pH = 7. The volume of methanol was reduced under vacuum and the organic phase was extracted with CH_2Cl_2. The crude mixture was purified by column chromatography (10:1to 4:1 hexane-EtOAc) to afford **137** as a colorless oil (380 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.72 (t, *J* = 7.8 Hz, 1H), 4.22 (dt, *J* = 6.1, 2.0 Hz, 2H), 3.75 (s, 6H), 2.82 (t, *J* = 2.0 Hz, 2H), 2.77 (d, *J* = 7.6 Hz, 2H), 1.75 (s, 2H), 1.68-1.62 (br s, 1H), 1.64 (s, 3H), 1.53-1.41 (m, 6H), 1.37-1.26 (m, 6H), 0.97-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69, 140.90, 112.03, 81.31, 81.28, 57.39, 52.66, 51.20, 31.11, 29.13 (^3J(^{119}Sn-C) = 19 Hz), 27.38 (^2J(^{119}Sn-C) = 53 Hz), 22.76, 22.61, 18.77, 13.70, 9.45 (^1J(^{119}Sn-C) = 314, (^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{26}H_{46}O_5Na^{120}Sn$ $[M+Na]^+$: 581.2265. Found: 581.2245.

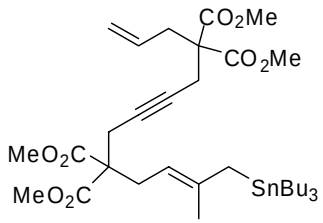
Dimethyl 2-(4-Methanesulfonyl-2-butynyl)-2-((*E*)-3-methyl-4-tri-*n*-butylstannyl-2-butenyl)malonate (138).



To a solution of **137** (350 mg, 0.63 mmol) in diethyl ether (15 mL) was added triethylamine (0.43 mL, 3.13 mmol). The mixture was cooled to 0ºC and methanesulfonyl chloride was slowly added (0.072 mL, 0.94 mmol). The mixture was stirred at 23ºC for 2 h, and was quenched by addition of water and subjected to usual extractive workup (Et_2O/H_2O/brine). The crude was purified by column chromatography (3:1to 2:1 hexane-EtOAc) to afford **138** as a colorless oil (350 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (t, *J* = 2.0 Hz, 2H), 4.71 (t, *J* = 7.6 Hz, 1H), 3.75 (s, 6H), 3.11 (s, 3H), 2.86 (t, *J* = 2.3 Hz, 2H), 2.75 (d, *J* = 7.6 Hz, 2H), 1.75 (s,

2H), 1.63 (s, 3H), 1.53-1.42 (m, 6H), 1.37-1.26 (m, 6H), 0.97-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.53, 141.29, 111.66, 85.88, 75.02, 58.00, 57.19, 52.76, 38.96, 31.36, 29.11 (^3J(^{119}Sn-C) = 20 Hz), 27.37 (^2J(^{119}Sn-C) = 55 Hz), 22.68, 22.62, 18.17, 13.70, 9.47 (^1J(^{119}Sn-C) = 314, (^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{27}H_{48}O_7SNa^{120}Sn$ $[M+Na]^+$: 659.2040. Found: 659.2047.

(*E*)-Tetramethyl 12-methyl-13-(tri-*n*-butylstannyl)trideca-1,11-dien-6-yne-4,4,9,9-tetracarboxylate (131).

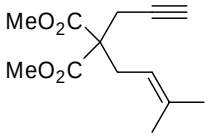


This compound was prepared from **138** and dimethyl allyl malonate following the general procedure for alkylation. After purification by column chromatography (10:1 to 8:1 hexane-EtOAc) the title compound was obtained as a colorless oil (79%).^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (ddt, *J* = 16.9, 10.1, 7.6 Hz, 1H), 5.19 (dd, *J* = 16.9, 2.0 Hz, 1H), 5.13 (dd, *J* = 9.9, 2.0 Hz, 1H), 4.72 (t, *J* = 8.2 Hz, 1H), 3.74 (s, 6H), 3.73 (s, 6H), 2.80-268 (m, 8H), 1.74 (s, 2H), 1.62 (s, 3H), 1.55-1.41 (m, 6H), 1.37-1.25 (m, 6H), 0.97-0.72 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.61, 170.22, 140.68, 131.91, 119.68, 112.26, 78.41, 77.23, 57.42, 57.01, 52.66, 52.56, 36.42, 30.96, 29.12 (^3J(^{119}Sn-C) = 20 Hz), 27.37 (^2J(^{119}Sn-C) = 55 Hz), 22.90, 22.67, 22.59, 18.74, 13.69, 9.42 (^1J(^{119}Sn-C) = 313, (^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{34}H_{56}O_8Na^{120}Sn$ $[M+Na]^+$: 735.2895. Found: 735.2908.

Synthesis of 1,6-enynes 141, 144 and 146.

The synthesis of these compounds was carried out according to reported procedures.

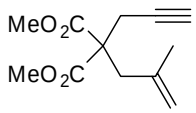
Dimethyl 2-(3-methyl-2-butenyl)-2-(2-propynyl)malonate (141).[67]



67 Trost, B. M.; Braslau, R. *Tetrahedron Lett*. **1988**, *29*, 1231-1234.

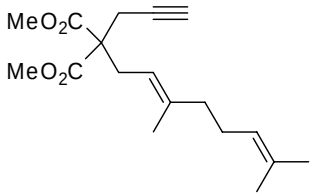
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (t, *J* = 7.6 Hz, 1H), 3.75 (s, 6H), 2.79 (m, 4H), 2.02 (t, *J* = 2.0 Hz, 1H), 1.71 (s, 3H), 1.67 (s, 3H).

Dimethyl 2-(2-methyl-2-propenyl)-2-(2-propynyl)malonate (144).[68]



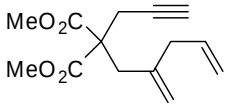
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93 (t, *J* = 1.5 Hz, 1H), 4.86 (s, 1H), 3.76 (s, 6H), 2.86 (m, 4H), 2.05 (t, *J* = 3.5 Hz, 1H), 1.67 (s, 3H). Deuterated enyne **144**-d_1 was obtained by deprotonation with *n*-BuLi in THF at -78ºC and subsequent quenching with D_2O. Disappearance of the alkynyl hydrogen signal at 2.05 ppm on the ^{1}H NMR spectra was observed.

Dimethyl (3,7-dimethyl-octa-2*E*,6-dienyl)-(2-propynyl)malonate (146).[69]



^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (t, *J* = 7.0 Hz, 1H), 4.93 (*J* = 7.6 Hz, 1H), 3.76 (s, 6H), 2.80 (m, 4H), 2.13-1.97 (m, 5H), 1.70 (s, 3H), 1.67 (s, 3H), 1.62 (s, 3H).

Dimethyl 2-(2-methylenepent-4-enyl)-2-(2-propynyl)malonate (148).



To a solution of $Pd[(PPh_3)]_4$ (230 mg, 0.2 mmol) in toluene (7 mL) was added dimethyl 2-(2-bromoallyl)malonate[54] (1 g, 4 mmol) in toluene (3 mL). The mixture was stirred under reflux for 2 h, the toluene was removed under reduced pressure and the residue was purified by distillation. The product resulting from the coupling distilled between 100-110ºC (3 mm Hg) along with part of tributyltinbromide generated in the reaction. The mixture (760 mg) was added to a suspension of NaH (60% in mineral oil, 133 mg, 3.32 mmol) in DMF (15 mL) at 0ºC, and after 10 minutes propargyl bromide (0.54 mL, 6.04 mmol) was added. The resulting yellow solution was stirred at 23ºC for

68 Trost, B. M.; Tanory, G. T. *J. Am. Chem. Soc*. **1998**, *110*, 1636-1638.

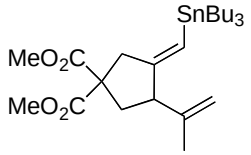
69 Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc*. **1991**, *113*, 636-644.

1 h and then subjected to the usual extractive workup (Et_2O/H_2O). The crude material was purified by column chromatography (10:1 hexane-EtOAc) after deactivation of the silica with triethylamine (5%) to yield **148** as yellowish oil, (560 mg, 57% over the two steps). ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.78 (tdd, *J* = 16.7, 10.3, 6.7 Hz, 1H), 5.10-4.92 (m, 4H), 3.76 (s, 6H), 2.90-2.85 (m, 4H), 2.67 (d, *J* = 6.7 Hz, 2H), 2.06 (t, *J* = 2.6 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.48, 142.29, 135.73, 116.68, 116.24, 79.11, 71.85, 56.69, 52.78, 41.04, 37.31, 22.73. HRMS-ESI Calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$: 273.1103. Found: 273.1009.

General procedure for the silver-catalyzed cyclizations of allylstannane-alkynes

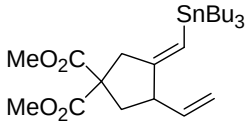
To a suspension of the silver salt or complex (0.01 mmol) in toluene (2 mL) at 70ºC (unless otherwise stated) was added the substrate (0.1 mmol) dissolved in toluene (1 mL). The reaction was stirred at this temperature for the stated reaction times, the mixture was cooled to room temperature and filtered through a pad of Celite. The pad was washed with Et_2O, the combined solvent were evaporated and the residue was purified by column chromatography (hexane-EtOAc).

Dimethyl 4-(1-methylethenyl)-3-[(*E*)-tri-*n*-butylstannylmethylene]cyclopentane-1,1-dicarboxylate (87).[44c]



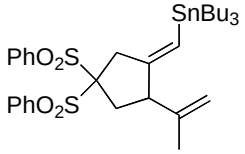
^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.65 (q, *J* = 1.9 Hz, $^2J(^{119}$Sn-H) = 63.5 Hz, 1H), 4.85 (m, 1H), 4.83 (m, 1H), 3.76 (s, 6H), 3.39-3.27 (m, 1H), 3.00, 2.91 (AB doublet of triplets, J_{AB} = 16.5, *J* = 2.6 Hz, 2H), 2.57 (ddd, *J* = 12.9, 7.9, 1.8 Hz, 1H), 2.13 (dd, J_1 = 12.8, 11.4, Hz, 1H), 1.63 (s, 3H), 1.59-1.43 (m, 6H), 1.38-1.25 (m, 6H), 1.03-0.83 (m, 15H).

Dimethyl 4-ethenyl-3-[(*E*)-tri-*n*-butylstannylmethylene]cyclopentane-1,1-dicarboxylate (98).[46]



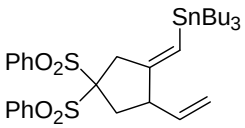
^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.68 (q, J = 2.3 Hz, $^{2}J(^{119}$Sn-H) = 61.8 Hz, 1H), 5.63 (ddd, J_1 = 17.1, 10.2, 8.2 Hz, 1H), 5.11-5.00 (m, 2H), 3.76 (s, 3H), 3.75 (s, 3H), 3.26-3.13 (m, 1H), 3.02, 2.91 (AB doublet of triplets, J_{AB} = 16.6, J = 2.3 Hz, 2H), 2.63 (ddd, J =12.8, 7.7, 1.5 Hz, 1H), 2.04 (dd, J= 12.9, 11.0 Hz, 1H), 1.63-1.39 (m, 6H), 1.38-1.26 (m, 6H), 1.03-0.82 (m, 15H).

1,1-Bis(phenylsulfonyl)-4-(1-methylethenyl)-3-[(*E*)-tri-*n*-butylstannylmethylene]cyclopentane (100).



Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.17–8.02 (m, 4H), 7.79-7.69 (m, 2H), 7.67-7.56 (m, 4H), 5.68 (q, J = 2.3 Hz, $^{2}J(^{119}$Sn-H) = 56.3 Hz, 1H), 4.90 (s, 1H), 4.83 (s, 1H), 3.56 (t, J = 9.7 Hz, 1H), 3.39, 3.16 (AB doublet of triplets, J_{AB} = 18.4, J = 2.3 Hz, 2H), 2.74 (dd, J = 15.0, 11.3 Hz, 1H), 2.56 (dd, J = 14.6, 8.3 Hz, 1H), 1.57 (s, 3H), 1.55-1.42 (m, 6H), 1.37-1.26 (m, 6H), 1.03-0.82 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.84, 143.89, 136.94, 136.06, 134.66, 134.54, 131.24, 131.14, 128.78, 128.71, 121.28, 115.30, 91.85, 54.34, 39.66, 35.47, 29.17 ($^{3}J(^{119}$Sn-C) = 20 Hz), 27.30 ($^{2}J(^{119}$Sn-C) = 55 Hz), 17.12, 13.70, 9.82 ($^{1}J(^{119}$Sn-C) = 342, $^{1}J(^{117}$Sn-C) = 327 Hz). Anal. Calcd for $C_{33}H_{48}O_4S_2Sn$: C, 57.31; H, 7.00; S, 9.27. Found: C, 57.22; H, 6.81; S, 8.99. HRMS-ESI Calcd for $C_{33}H_{48}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 715.1914. Found: 715.1897.

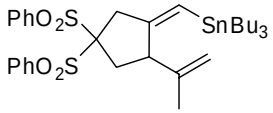
1,1-Bis(phenylsulfonyl)-4-ethenyl-3-[(*E*)-tributylstannylmethylene]cyclopentane (101).



Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.14-8.02 (m, 4H), 7.82-7.69 (m, 2H), 7.67-7.56 (m, 4H), 5.72 (q, J = 2.3 Hz, $^{2}J(^{119}$Sn-H) = 55.3 Hz, 1H), 5.56 (ddd, J = 17.0, 10.1, 8.4 Hz,1H), 5.15 (dd, J = 9.9, 1.7 Hz, 1H), 5.06 (dd, J = 17.0, 1.4 Hz, 1H), 3.41 (br q, J = 8.7 Hz, 1H), 3.33, 3.22 (AB doublet of triplets, J_{AB} = 18.6, J = 2.1 Hz, 2H), 2.66 (dd, J= 14.8, 8.4 Hz, 1H), 2.56 (dd, J = 14.8, 11.3 Hz, 1H), 1.58- 1.43 (m, 6H), 1.38-1.27 (m, 6H), 1.00-0.83 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.62, 138.47, 136.89, 136.03, 134.68, 134.54, 131.26, 131.21, 128.78, 128.67, 121.82,

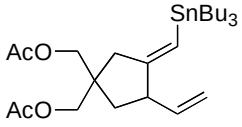
117.71, 91.67, 50.72, 39.17, 37.55, 29.14 (^3J(^{119}Sn-C) = 20 Hz), 27.31 (^2J(^{119}Sn-C) = 57 Hz), 13.68, 9.81 (^1J(^{119}Sn-C) = 343, ^1J(^{117}Sn-C) = 327 Hz). HRMS-ESI Calcd for $C_{32}H_{46}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 701.1757. Found: 701.1791.

1,1-Bis(phenylsulfonyl)-4-(1-methylethenyl)-3-[(*Z*)-tri-*n*-butylstannylmethylene]cyclopentane (125).



To a solution of $[Pd_2(dba)_3]$·dba (3.32 mg, 2.8 10^{-3} mmol) in dioxane (3 mL) was added (*E*)-**88** (85 mg, 0.12 mmol) in 1,4-dioxane (2 mL). The solution was heated at 60ºC for 2 h after which it was cooled to room temperature and filtered through a pad of Celite. The pad was washed with Et_2O and the filtrates were concentrated to give a residue that was further purified by column chromatography (10:1 hexane-EtOAc) to yield **125** as a vitreous solid, (76 mg, 87%).^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.12–7.99 (m, 4H), 7.77-7.68 (m, 2H), 7.65-7.52 (m, 4H), 5.87 (s, ^2J(^{119}Sn-H) = 50.9 Hz, 1H), 4.86 (s, 1H), 4.79 (s, 1H), 3.75 (d, *J* = 17.5 Hz, 1H), 3.44 (t, *J* = 9.3 Hz, 1H), 2.89 (dd, *J* = 14.6, 9.9 Hz, 1H), 2.79 (d, *J*= 17.5 Hz, 1H), 2.63 (dd, *J* = 14.6, 9.9 Hz, 1H), 1.71 (s, 3H), 1.54-1.42 (m, 6H), 1.38-1.26 (m, 6H), 0.97-0.82 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.91, 146.15, 137.42, 136.08, 134.58, 134.42, 131.04, 130.98, 128.65, 128.62, 124.96, 113.49, 92.13, 51.56, 43.56, 37.35, 29.16 (^3J(^{119}Sn-C) = 20 Hz), 27.39 (^2J(^{119}Sn-C) = 57 Hz), 18.55, 13.72, 10.15 (^1J(^{119}Sn-C) = 345, ^1J(^{117}Sn-C) = 330 Hz). HRMS-ESI Calcd for $C_{33}H_{48}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 715.1914. Found: 715.1938.

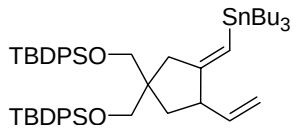
1,1-Bis(acetoxymethyl)-4-ethenyl-3-[(*E*)-tributylstannylmethylene]cyclopentane (107).



Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.73-5.67 (m, 1H), 5.64 (ddd, *J* = 16.9, 10.1, 8.1 Hz, 1H), 5.10-4.99 (m, 2H), 4.07, 3.96 (AB system, J_{AB} = 11.1 Hz, 2H), 4.05, 3.98 (AB, J_{AB} = 11.1 Hz, 2H) 3.20 (br q, *J* = 8.8 Hz, 1H), 2.28 (m, 2H), 2.09 (s, 3H), 2.08 (s, 3H), 1.96 (dd, *J* = 13.2, 8.3 Hz, 1H), 1.60-1.40 (m, 6H), 1.37-1.25 (m, 6H), 1.01-0.81 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.03, 170.98, 160.39, 140.57, 120.87, 115.32, 67.67, 65.86, 49.57, 44.10, 40.97, 38.24, 29.18 (^3J(^{119}Sn-C) = 20 Hz),

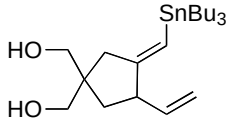
27.29 (^2J(^{119}Sn-C) = 55 Hz), 20.84, 20.82, 13.67, 9.79 (^1J(^{119}Sn-C) = 341, ^1J(^{117}Sn-C) = 325 Hz). HRMS-ESI Calcd for $C_{26}H_{46}O_4Na^{120}Sn$ $[M+Na]^+$: 565.2316. Found: 565.2298.

1,1-Bis(*tert*-butyldiphenylsilyloxymethyl)-4-ethenyl-3-[(*E*)-tri-*n*-butylstannylmethylene]cyclopentane (106).



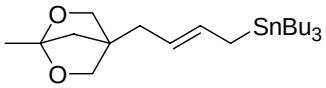
Colorless oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.87-7.56 (m, 8H), 7.54-7.30 (m, 12H), 5.55 (overlapping s, ^2J(^{119}Sn-H) = 68.1 Hz, 1H), 5.55 (m, 1H), 5.00 (d, J = 9.9 Hz, 1H), 4.92(d, J = 16.7 Hz, 1H), 3.80, 3.57 (AB system, J_{AB} = 9.4 Hz, 2H), 3.76, 3.59 (AB, J_{AB} = 9.7 Hz, 2H), 2.95 (br q, J = 8.3 Hz, 1H), 2.31 (m, 2H), 1.96 (dd, J = 12.7, 8.2 Hz, 1H), 1.68-1.22 (m, 14H), 1.08 (s, 18H), 0.95-0.81 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.92, 141.44 135.70, 135.69, 133.79, 133.70, 129.58, 129.53, 127.64, 118.72, 114.70, 67.4, 65.34, 50.02, 48.65, 41.19, 37.23, 29.23 (^3J(^{119}Sn-C) = 20 Hz), 27.29, 26.98, 26.93, 19.42, 19.40 13.70, 9.74 (^1J(^{119}Sn-C) = 336, ^1J(^{117}Sn-C) = 323 Hz). Anal. Calcd for $C_{54}H_{78}O_2SnSi_2$: C, 69.44; H, 8.42. Found: C, 69.62; H, 7.99. HRMS-ESI Calcd for $C_{54}H_{78}O_2Na^{120}SnSi_2$ $[M+Na]^+$: 957.4460. Found: 957.4496.

1,1-Bis(hydroxymethyl)-4-ethenyl-3-[(*E*)-tributylstannylmethylene]cyclopentane (103).



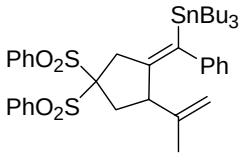
Yellowish oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 575-5.54 (m, 2H), 5.09-4.99 (m, 2H), 3.74-3.60 (m, 4H), 3.18 (br q, J = 8.2 Hz, 1H), 2.52 (br s, 1H), 2.40 (br s, 1H), 2.24, 2.15 (AB doublet of triplets, J_{AB} = 16.6, J = 1.9 Hz, 2H), 2.04 (dd, J = 13.1, 8.4 Hz, 1H), 1.60-1.42 (m, 6H), 1.37 (dd, J = 13.1, 10.4 Hz, 1H), 1.37-1.26 (m, 6H), 1.09-0.79 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 161.58 (C), 141.05 (CH), 119.97 (CH), 115.07 (CH_2), 71.18 (CH_2), 68.64 (CH_2), 49.71 (CH), 46.74 (C), 40.91 (CH_2), 37.71 (CH_2), 29.20 (CH_2, ^3J(^{119}Sn-C) = 20 Hz), 27.29 (CH_2, ^2J(^{119}Sn-C) = 52 Hz), 13.71 (CH_3), 9.80 (CH_2, ^1J(^{119}Sn-C) = 340, ^1J(^{117}Sn-C) = 324 Hz). HRMS-ESI Calcd for $C_{22}H_{42}O_2Na^{120}Sn$ $[M+Na]^+$: 481.2104. Found: 481.2085.

1-Methyl-4-[(*E*)-4-tri-*n*-butylstannyl-2-butenyl]-2,6-dioxabicyclo[2.2.1]heptane (105).



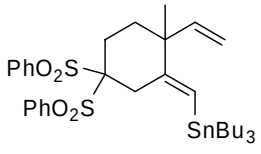
Colorless oil: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 575-5.52 (m, 1H), 5.24-5.00 (m, 1H), 3.78, 3.74 (AB, J_{AB} = 5.7 Hz, 2H), 3.83- 3.71 (m, 2H), 2.27 (d, J = 7.3 Hz, 2H), 1.80-1.66 (m, 4H), 1.55 (s, 3H), 1.55-1.43 (m, 6H), 1.38-1.24 (m, 6H), 0.98-.79 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 133.00 (C), 119.68 (C), 108.38 (C), 76.50 (CH_2), 49.52 (C), 44.35 (CH_2), 31.76 (CH_2), 29.12 (CH_2, ^{3}J(^{119}Sn-C) = 20 Hz), 27.23 (CH_2,^{2}J(^{119}Sn-C) = 52 Hz), 18.04 (CH_3), 14.20 (CH_2), 13.78 (CH_3), 9.17 (CH_2, ^{1}J(^{119}Sn-C) = 317, ^{1}J(^{117}Sn-C) = 300 Hz). HRMS-ESI Calcd for $C_{22}H_{42}O_2Na^{120}Sn$ $[M+Na]^+$: 481.2104. Found: 481.2082.

1,1-Bis(phenylsulfonyl)-4-(1-methylethenyl)-3-[(*E*)-tri-*n*-butylstannylphenylmethylene]cyclopentane (110).



Vitreous solid: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.14-8.03 (m, 4H), 7.82-7.69 (m, 2H), 7.69-7.56 (m, 4H), 7.21-7.11 (m, 2H), 7.09-6.99 (m, 1H), 6.85-6.75 (m, 2H), 4.24 (s, 1H), 4.12 (s, 1H), 3.78 (dt, J = 9.0, 2.1 Hz, 1H), 3.58 (dd, J = 17.4, 2.5 Hz, 1H), 3.16 (d, J = 17.4 Hz, 1H), 2.65 (d, J = 9.3 Hz, 2H), 1.49-1.34 (m, 9H), 1.30-1.18 (m, 6H), 0.94-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 148.32 (C), 144.92 (C), 144.22 (C), 141.97 (C), 137.01 (C), 136.56 (C), 134.60 (CH), 134.52 (CH), 131.30 (CH), 131.00 (CH), 128.84 (CH), 128.74 (CH),127.78 (CH), 126.39 (CH), 124.65(CH), 113.19 (CH_2), 92.26 (C), 50.31 (CH), 41.40 (CH_2), 36.25 (CH_2), 29.04 (CH_2,^{3}J(^{119}Sn-C) = 19 Hz), 27.32 (CH_2,^{2}J(^{119}Sn-C) = 60 Hz), 17.83 (CH_3), 13.67 (CH_3), 10.54 (CH_2, ^{1}J(^{119}Sn-C) = 330, ^{1}J(^{117}Sn-C) = 316 Hz). HRMS-ESI Calcd for $C_{39}H_{52}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 791.2227. Found: 791.2253.

1,1-Bis(phenylsulfonyl)-5-ethenyl-5-methyl-4-[(*E*)-tri-*n*-butylstannylmethylene]cyclohexane (112).

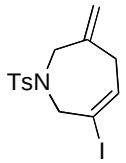


White solid, mp 121-123ºC: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.15-8.08 (m, 2H), 8.06-8.02 (m, 2H), 7.76-7.68 (m, 2H), 7.66-7.56 (m, 4H), 5.81 (overlapping s, $^{2}J(^{119}$Sn-H) = 56.2 Hz, 1H), 5.81 (overlapping dd, J= 17.3, J_2 = 10.6 Hz, 1H), 5.06 (dd, J = 10.5, 1.1 Hz, 1H), 5.01 (dd, J = 17.4, 1.1 Hz, 1H), 3.09, 2.98 (AB, J_{AB} = 15.5, 2H), 2.49 (ddd, J = 15.3, 10.4, 4.7 Hz, 1H), 2.27 (dt, J = 15.7, 4.9 Hz, 1H), 2.03-1.83 (m, 2H),1.53-1.37 (m, 6H), 1.33-1.21 (m, 9H), 0.90-0.74 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 152.66 (C), 145.80 (CH), 136.63 (C), 136.31 (C), 134.34 (CH), 134.28 (CH), 131.56 (CH), 131.40 (CH), 128.48 (CH), 125.91 (CH), 113.29 (CH_2), 89.06 (C), 44.42 (C), 35.10 (CH_2), 33.89 (CH_2), 29.15 (CH_2, $^{3}J(^{119}$Sn-C) = 20 Hz), 27.26 (CH_2,$^{2}J(^{119}$Sn-C) = 50 Hz), 26.56 (CH_3), 22.04 (CH_2), 13.77 (CH_3), 10.07 (CH_2, $^{1}J(^{119}$Sn-C) = 341, $^{1}J(^{117}$Sn-C) = 325 Hz). Anal. Calcd for $C_{34}H_{50}O_4S_2Sn$: C, 57.87; H, 7.14; S, 9.09. Found: C, 57.66; H, 6.87; S, 9.05. HRMS-ESI Calcd for $C_{34}H_{50}O_4NaS_2{}^{120}Sn$ $[M+Na]^+$: 729.2070. Found: 729.2053.

Cyclization of sulfonamide 95

To a suspension of the silver complex **109**, (20 mg, 0.03 mmol) in toluene (2 mL) at 70 ºC was added **95** (150 mg, 0.28 mmol) dissolved in toluene (1.5 mL). The reaction was stirred at 70ºC for 30 min, was then cooled to room temperature and filtered through a pad of Celite. The pad was washed with Et_2O and the filtrate was evaporated and purified by column chromatography (20:1, hexane-EtOAc), to yield a mixture of two inseparable stannanes. The mixture was treated with I_2 (140 mg, 0.57 mmol) in THF (5 mL) for 2 h, then was diluted with Et_2O and washed with sodium thiosulfate (10%). The organic phase was dried over anhydrous $MgSO_4$, evaporated and purified by column chromatography (10:1, hexane-EtOAc) to yield **114** (48 mg, 43%) and **115** (31 mg, 27%).

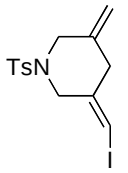
6-Iodo-3-methylene-1-(*p*-toluene-4-sulfonyl)-2,3,4,7-tetrahydro-1*H*-azepine (114).



White solid; mp 132-134ºC: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.73 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 6.29 (tt, J = 5.7, J = 1.6 Hz, 1H), 4.92 (s, 1H), 4.90 (d, J = 0.8 Hz, 1H), 4.16 (d, J = 1.4 Hz, 2H), 4.02 (s, 2H), 2.77 (d, J = 5.8 Hz 2H), 2.45 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 143.66 (C), 142.86 (C), 138.63 (CH),

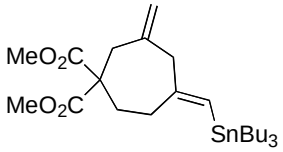
129.74 (CH), 127.11 (CH), 113.99 (CH_2), 93.52 (C), 57.78 (CH_2), 54.52 (CH_2), 37.40 (CH_2), 21.57 (CH_3). HRMS-ESI Calcd for $C_{14}H_{16}NO_2NaSI$ $[M+Na]^+$: 411.9844. Found: 411.9856. The structure was confirmed by COSY, HMQC, and HMBC experiments.

(*E*)-3-Iodomethylene-5-methylene-1-(*p*-toluene-4-sulfonyl)piperidine (115).



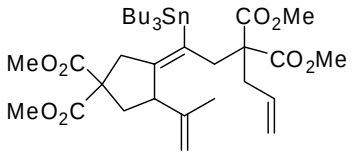
White solid, mp 130-132ºC; ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.04 (t, J= 1.3 Hz, 1H), 4.87 (d, J = 0.9 Hz, 1H), 4.85 (d, J = 0.9 Hz, 1H), 3.89 (s, 2H), 3.82 (s, 2H), 2.96 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 143.75 (C), 141.62 (C), 138.26 (C), 134.18 (C), 129.70 (CH), 127.85 (CH), 111.60 (CH_2), 74.99 (CH), 52.89 (CH_2), 50.80 (CH_2), 41.69 (CH_2), 21.64 (CH_3). Anal. Calcd for $C_{14}H_{16}NO_2SI$: C, 43.20; H, 4.14; N, 3.60; S, 8.24. Found: C, 43.21; H, 4.10; N, 3.76; S, 8.29. HRMS-ESI Calcd for $C_{14}H_{16}NO_2NaSI$ $[M+Na]^+$: 411.9844. Found: 411.9840. The structure was confirmed by COSY, HMQC, and HMBC experiments.

Dimethyl 4-[(*E*)-tri-*n*-butylstannylmethylene]-6-methylenecycloheptane-1,1-dicarboxylate (116).



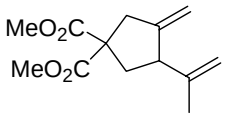
Colorless oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.59 (s, ^2J(^{119}Sn-H) = 62.1 Hz, 1H), 4.90 (d, J = 1.7 Hz, 1H), 4.85 (s, 1H), 3.73 (s, 6H), 3.20 (d, J = 1.1 Hz, 2H), 2.78 (s, 2H), 2.38-2.29 (m, 2H), 2.10-2.03 (m, 2H), 1.56-1.41 (m, 6H), 1.38-1.25 (m, 6H), 0.99-.79 (m, 15H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) 171.88 (C), 156.47 (C), 142.99 (C), 125.40 (CH), 115.53 (CH_2), 52.80 (C), 52.39 (CH_3), 49.56 (CH_2), 39.05 (CH_2), 35.80 (CH_2), 33.80 (CH_2), 29.10 (CH_2,^3J(^{119}Sn-C) = 27 Hz), 27.33 (CH_2,^2J(^{119}Sn-C) = 57 Hz), 13.70 (CH_3), 10.07 (CH_2, ^1J(^{119}Sn-C) = 339, ^1J(^{117}Sn-C) = 323 Hz). Anal. Calcd for $C_{25}H_{44}O_4Sn$: C, 56.94; H, 8.41. Found: C, 57.28; H, 8.43. HRMS-ESI Calcd for $C_{25}H_{44}O_4Na^{120}Sn$ $[M+Na]^+$: 551.2159. Found: 551.2177.

Dimethyl 4-(1-methylethenyl)-3-[(*E*)-3,3-bis(methoxycarbonyl)-1-(tri-*n*-butylstannyl)5-hexenylidene)cyclopentane-1,1-dicarboxylate (139).



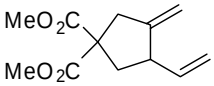
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.09-5.01 (m, 2H), 4.79 (s, 1H), 4.77 (s, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H), 3.44 (t, *J* = 7.8 Hz, 1H), 3.14 (m, 2H), 2.81-2.49 (m, 5H), 2.03 (dd, *J* = 12.8, 7.6 Hz, 1H), 1.71 (s, 3H), 1.59-1.43 (m, 6H), 1.41-1.25 (m, 6H), 1.07-0.86 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.80, 171.78, 171.63, 171.54, 154.49, 145.69, 134.72, 133.79, 118.10, 11.42, 59.25, 59.09, 52.80, 52.70, 52.16, 52.11, 48.62, 45.36, 39.61, 39.41, 37.98, 29.14, 27.56, 19.75, 13.69. HRMS-ESI Calcd for $C_{34}H_{56}O_8Na^{120}Sn$ $[M+Na]^+$: 735.2895. Found: 735.2871.

Dimethyl 3-methylene-4-(1-methylethenyl)cyclopentane-1,1-dicarboxylate (84).[70]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.03 (q, *J* = 2.2 Hz, 1H), 4.85 (m, 2H), 4.16 (q, *J* = 2.2 Hz, 1H), 3.76 (s, H), 3.74 (s, 3H), 3.34-3.25 (m, 1H), 3.08, 2.94 4.86 (AB doublet of quartets, J_{AB} = 16.8, *J* = 2.5 Hz, 2H), 2.54 (ddd, *J* = 13.0, 7.9, 1.6 Hz, 1H), 2.14 (dd, *J* = 12.9, 11.3 Hz, 1H), 1.66 (s, 3H).

Dimethyl 4-ethenyl-3-methylencyclopentane-1,1-dicarboxylate (99).[70, 71]

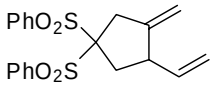


^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.66 (ddd, *J* = 17.5, 9.6, 8.0 Hz, 1H), 5.13-5.05 (m, 2H), 5.00 (q, *J* = 2.3 Hz, 1H), 4.84 (q, *J* = 2.3 Hz, 1H), 3.76 (s, H), 3.74 (s, 3H), 3.17 (br q, *J* = 8.1 Hz, 1H), 3.09, 2.97 (AB doublet of quartets, J_{AB} = 17.1, *J* = 2.3 Hz, 2H), 2.59 (ddd, *J* = 12.9, 7.8, 1.2 Hz, 1H), 2.03 (dd, *J* = 13.0, 10.9 Hz, 1H).

70 Castaño, A. M.; Ruano, M.; Echavarren, A. M. *Tetrahedron Lett*. **1996**, *37*, 6591-6594.

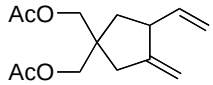
71 Oppolzer, W.; Fürstner, A. *Helv. Chim. Acta*. **1993**, *76*, 2329-2337.

1,1-Bis(phenylsulfonyl)-3-methylene-4-ethenylcyclopentane (102).[72]



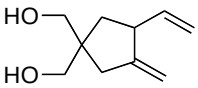
^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.13-8.02 (m, 4H), 7.79-7.69 (m, 2H), 7.67-7.56 (m, 4H), 5.57 (ddd, *J* = 17.1, 10.9, 8.3 Hz, 1H), 5.18-5.07 (m, 2H), 4.90 (q, *J* = 2.4 Hz, 1H), 4.78 (q, *J* = 2.3 Hz, 1H), 3.37 (br q, *J* = 8.8 Hz, 1H), 3.31 (m, 1H), 2.78 (dd, *J* = 15.2, 8.5 Hz, 1H), 2.50 (dd, *J* = 15.2, 10.7, 1H)

1,1-Bis(acetoxymethyl)-4-ethenyl-3-methylencyclopentane (108).



Colorless oil**:** ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.67 (ddd, J_1 = 17.5, 9.6, 8.1 Hz, 1H), 5.13-5.03 (m, 2H), 4.97 (m, 1H), 4.85 (m, 1H), 4.06, 3.97 (AB system, J_{AB} = 11.2 Hz, 2H), 4.05, 3.98 (AB, J_{AB} = 10.9 Hz, 2H), 3.19 (br q, *J* = 8.1 Hz, 1H), 2.34 (s, 2H), 2.09 (s, 3H), 2.08 (s, 3H), 1.96 (dd, *J* = 13.5, 8.5 Hz, 1H), 1.45 (dd, *J* = 13.3, 10.2 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 171.08 (C), 171.03 (C), 151.72 (C), 139.98 (CH), 115.45 (CH_2), 108.35 (CH_2), 67.64 (CH_2), 65.95 (CH_2), 47.05 (CH), 47.22 (C), 39.12 (CH_2), 38.20 (CH_2), 20.86 (CH_3). HRMS-CI Calcd for $C_{14}H_{19}O_4$ $[M-H]^+$: 251.1283. Found: 251.1275.

1,1-Bis(hydroxymethyl)-3-methylene-4-ethenylcyclopentane (104).[73]

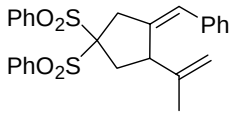


White solid**,** mp 53-55ºC: ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.69 (ddd, *J* = 16.5, 10.5, 7.9 Hz, 1H), 5.12-5.02 (m, 2H), 4.96 (m, 1H), 4.83 (m, 1H), 3.68 (m, 4H), 3.16 (br q, *J* = 8.6 Hz, 1H), 2.39-2.30 (m, 2H), 2.26 (dq, *J*= 16.6, 1.9 1H), 2.19 (t, *J* = 5.1 Hz, 1H), 2.00 (dd, *J* = 13.1, 8.5 Hz, 1H), 1.35 (dd, *J* = 13.2, 10.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 152.70 (C), 140.30 (CH), 115.13 (CH_2), 107.76 (CH_2), 71.10 (CH_2), 68.80 (CH_2), 47.09 (CH), 46.80 (C), 38.75 (CH_2), 37.83 (CH_2). HRMS-CI Calcd for $C_{10}H_{15}O_2$ $[M-H]^+$: 167.1072. Found: 167.1073.

72 Oppolzer, W.; Ruiz-Montes, J. *Helv. Chim. Acta* **1993**, *76*, 1266.

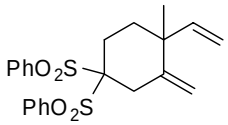
73 Kang, S.-K.; Ko, B.-S.; Lee, D.-M. *Tetrahedron Lett*. **2002**, *43*, 6693-6696.

1,1-Bis(phenylsulfonyl)-3-((*Z*)-bencylidene)-4-methylethenylcyclopentane (111).[43]



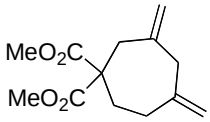
^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.17-8.08 (m, 2H), 8.07-8.01 (m, 2H), 7.80-7.71 (m, 1H), 7.70-7.60 (m, 3H), 7.58-7.50 (m, 2H), 7.32-7.24 (m, 2H), 7.24-7.13 (m, 3H), 6.32 (s, 1H), 4.76 (s, 2H), 3.83 (dt, *J* = 17.9, 2.2 Hz, 1H), 3.70 (t, *J* = 7.9 Hz, 1H), 3.05-2.94 (m, 2H), 2.74 (dd, *J* = 15.5, 6.9 Hz, 1H), 1.69 (s, 3H).

1,1-Bis(phenylsulfonyl)-4-ethenyl-4-methyl-3-methylidencyclohexane (113).[43]



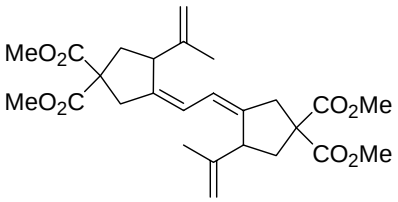
^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.13–8.08 (m, 2H), 8.03-7.99 (m, 2H), 7.76-7.69 (m, 2H), 7.65-7.56 (m, 4H), 5.71 (dd, *J* = 17.5, 10.6 Hz, 1H), 5.02-4.96 (m, 3H), 4.94 (dd, *J* = 17.4, 1.1 Hz, 1H), 3.13, 3.02 (AB doublet of triplets, J_{AB} = 15.7, *J* = 1.4 Hz, 2H), 2.43 (dd, *J* = 7.5, 5.6 Hz, 2H), 2.02-1.93 (m, 1H), 1.84 (dt, *J* = 13.8, 5.2 Hz, 1H), 1.18 (s, 3H).

Dimethyl 3,5-Dimethylenecycloheptane-1,1-dicarboxylate (117).



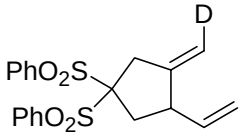
Colorless oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.93 (d, *J* = 1.6 Hz, 1H), 4.87 (s, 1H), 4.84 (s, 1H), 4.81 (d, *J* = 1.6 Hz, 1H), 3.73 (s, 6H), 3.08 (s, 2H), 2.77 (s, 2H), 2.41-2.32 (m, 2H), 2.13-2.06 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 172.20 (C), 147.68 (C), 142.63 (C), 115.95 (CH_2), 112.67 (CH_2), 52.41 (CH_3), 44.88 (CH_2), 39.00 (CH_2), 35.89 (CH_2), 31.86 (CH_2). HRMS-ESI Calcd for $C_{13}H_{18}O_4Na$ $[M+Na]^+$: 261.1103. Found: 261.1093.

Dimer 85.



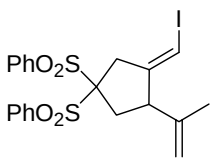
Colorless oil, 1.4:1 mixture of diastereomers. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 5.87-5.79 (br s, 2H), 4.93-4.88 (br s, 2H), 4.87 (s, 2H), 3.75 (s, 12H), 3.41-3.30 (m, 2H), 3.20, 2.91 (AB system, J_{AB} = 17.6 Hz, 2H), 2.56-2.46 (m, 2H), 2.18-2.06 (m, 2H), 1.64 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) Major diastereomer: δ 172.09 (C), 144.53 (C), 141.22 (C), 119.85 (CH), 114.22 (CH_2), 58.83 (C), 52.80 (CH_3), 51.84 (CH), 38.39 (CH_2), 37.75 (CH_2), 18.03 (CH_3). Minor diastereomer: δ 172.02 (C), 144.50 (C), 141.41 (C), 119.80 (CH), 114.24 (CH_2), 58.78 (C), 52.88 (CH_3), 51.86 (CH), 38.33 (CH_2), 37.68 (CH_2), 17.99 (CH_3). HRMS-ESI Calcd for $C_{26}H_{34}O_8Na$ $[M+Na]^+$: 497.2151. Found: 497.2145.

Deuterodestannylation of 123: 1,1-Bis(phenylsulfonyl)-3-((*E*)-1-deuteromethyliden)-4-ethenylcyclopentane (118).



To a solution of **101** (45 mg, 0.066 mmol) in CD_3OD (3 mL) was added 12 M DCl (0.013 mL, 0.16 mmol) at room temperature. The reaction mixture was stirred for 30 min, after which the solvent was evaporated and the crude mixture purified by column chromatography (4:1, hexane-EtOAc) to yield a white solid, (20 mg, 78%) with 81% deuterium incorporation. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.16-8.00 (m, 4H), 7.79-7.69 (m, 2H), 7.67-7.56 (m, 4H), 5.57 (ddd, *J* = 17.2, 10.3, 8.4 Hz, 1H), 5.18-5.07 (m, 2H), 4.76 (q, *J* = 2.2 Hz, 1H), 3.37 (br q, *J* = 8.7 Hz, 1H), 3.31 (m, 1H), 2.78 (dd, *J* = 15.1, 8.7 Hz, 1H), 2.50 (dd, *J* = 14.8, 10.6, 1H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 148.04 (C) 137.54 (CH), 136.55 (C), 136.13 (C), 134.74 (CH), 134.62 (CH), 131.29 (CH), 131.20 (CH), 128.80 (CH), 128.76 (CH), 117.70 (CH_2), 108.71 (CHD), 91.39 (C), 48.04 (CH), 37.98 (CH_2), 37.59 (CH_2). The configuration was assigned on the basis of a NOESY experiment.

1,1-Bis(phenylsulfonyl)-3-((*E*)-iodomethylene)-4-(1-methylethenyl)cyclopentane. (119).

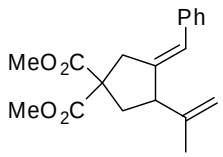


A solution of **100** (44.6 mg, 0.066 mmol) and I_2 (23 mg, 0.09 mmol) in THF (4 mL) was stirred at rt for 3 h. The mixture was diluted with Et_2O and washed with sodium thiosulfate (10%). The organic phase was dried over anhydrous $MgSO_4$, concentrated and purified by column chromatography (8:1 hexane-EtOAc) to yield **119** as a white solid (25 mg, 71%), mp 180-182ºC. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.12-8.05 (m, 4H), 7.80-7.72 (m, 2H), 7.68-7.59 (m, 4H), 5.94 (q, *J* = 2.4 Hz, 1H), 4.92 (s, 1H), 4.86 (s, 1H), 3.58 (br t, *J* = 9.9 Hz, 1H), 3.41, 3.25 (AB of triplets, J_{AB} = 19.5, *J* = 2.5 Hz, 2H), 2.87-2.73 (m, 2H), 1.57 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 151.87 (C) 142.52 (C), 136.54 (C), 135.58 (C), 134.95 (CH), 134.78 (CH), 131.28 (CH), 131.10 (CH), 128.98 (CH), 128.95 (CH), 115.78 (CH_2), 90.82 (C), 73.49 (CH), 52.89 (CH), 42.47 (CH_2), 36.85 (CH_2), 17.85 (CH_3). HRMS-ESI Cald for $C_{21}H_{21}O_4NaS_2I$ $[M+Na]^+$: 550.9824. Found: 550.9806.

Procedure for the Stille Coupling of 83 and 100 with iodobenzene

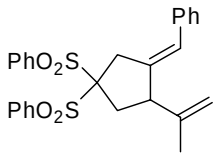
To a suspension of $[Pd(PPh_3)]_4$ (0.01 mmol), CuI (0.01 mmol), and CsF (0.4 mmol) in THF (3 mL) was added iodobenzene (0.3 mmol) and **83** or **100** (0.1 mmol) dissolved in THF (0.5 mL). The reaction mixture was stirred at 60ºC for the time indicated in Scheme 52, was then cooled to room temperature and filtered through a pad of Celite. This pad was washed with Et_2O and the filtrate was evaporated and purified by column chromatography (hexane-EtOAc).

Dimethyl 3-[(*E*)-bencylidene]-4-(1-methylethenyl)cyclopentane-1,1-dicarboxylate. (120).



Colorless oil. ^{1}H NMR (400 MHZ, $CDCl_3$) δ 7.39-7.29 (m, 4H), 7.24-7.19 (m, 1H), 6.21 (q, *J* = 2.6 Hz, 1H), 4.95 (s, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 3.57-3.48 (m, 1H), 3.44, 3.20 (AB doublet of triplets, J_{AB} = 17.6, *J* = 2.8 Hz, 2H), 2.57 (ddd, *J* = 12.8, 7.5, 1.5 Hz, 1H), 2.17 (dd, *J* = 12.6, 11.8 Hz, 1H), 1.71 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 172.00 (C), 171.96 (C), 144.84 (C), 142.19 (C), 137.84 (C), 128.31 (CH), 128.25 (CH), 126.38 (CH), 123.69 (CH), 114.43 (CH_2), 59.52 (C), 53.11 (CH), 52.90 (CH_3), 52.87 (CH_3), 39.26 (CH_2), 37.82 (CH_2), 18.00 (CH_3). HRMS-ESI Calcd for $C_{19}H_{22}O_4Na$ $[M+Na]^+$: 337.1416. Found: 337.1410.

1,1-Bis(phenylsulfonyl)-3-[(*E*)-bencylidene]-4-methylethenylcyclopentane (121).[74]



^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.05-7.98 (m, 2H), 7.94-7.88 (m, 2H), 7.73-7.66 (m, 1H), 7.66-7.60 (m, 1H), 7.57-7.50 (m, 2H), 7.44-7.32 (m, 4H), 7.30-7.24 (m, 1H), 7.20-7.15 (m, 2H), 6.22 (d, J = 1.8 Hz, 1H), 4.92 (s, 2H), 3.74-3.70 (m, 1H), 3.72, 3.40 (AB, J_{AB} = 18.9 Hz, 2H), 2.72, 2.63 (AB doublet of doublets, J_{AB} = 14.8, J = 8.7 Hz, 2H), 1.68 (s, 3H).

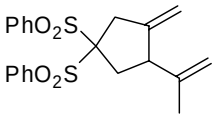
General procedure for asymmetric cyclizations of Table 4

To a suspension of the chiral silver catalyst (5 mol%) in toluene (0.5 mL) at the stated temperature, was added (*E*)-**88** (0.05 mmol) dissolved in toluene (0.7 mL). The reaction was stirred untill finished and then was filtered through a pad of Celite. The pad was washed with Et_2O, and the filtrate was evaporated and purified by column chromatography (8:1 to 6:1, hexane-EtOAc). Along with **100** was isolated **124** in the following yields: 37% (Table 3, entry 1), 7% (entry 2), 5% (entry 3), 7% (entry 5), and 10% (entry 6).

The enantiomeric ratio was determined at 27-30ºC, in a *Daicel ChiralPack AD* column (99:1 hexane-*i*-PrOH, flow = 0.7 mL/min; λ = 254 nm). Retention times: 10.6 (minor) and 11.6 min (major) (variations of room temperature caused small variation of retentions times. Average difference in retention times = 1.1 min).

A sample of **123** with 75% ee showed $[\alpha]_D^{25}$ = +3.12 (c = 1, CH_2Cl_2).

1,1-Bis(phenylsulfonyl)-4-methylethenyl-3-methylidencyclopentane (124).[43]

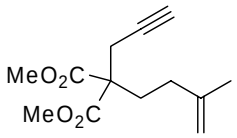


^{1}H NMR (400 MHZ, $CDCl_3$) δ 8.13-8.03 (m, 4H), 7.79-7.69 (m, 2H), 7.67-7.58 (m, 4H), 4.98 (q, J = 2.3 Hz, 1H), 4.89 (m, 1H), 4.86 (m, 1H), 4.80 (q, J = 2.3 Hz, 1H),

74 Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am, Chem. Soc*. **2001**, *123*, 10511-10520.

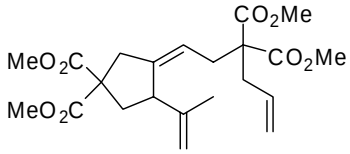
3.53 (m, 1H), 3.43, 3.22 (AB doublet of quartets, J_{AB} = 18.4, J = 2.0 Hz, 2H), 2.67 (d, J = 10.0 Hz, 2H), 1.59 (s, 3H).

Dimethyl 2-(3-methyl-3-butenyl)-2-(2-propynyl)malonate (130).



^{1}H NMR (400 MHZ, $CDCl_3$) δ 4.76 (s, 1H), 4.74 (s, 1H), 3.76 (s, 6H), 2.87 (d, J = 2.9 Hz, 2H), 2.27-2.19 (m, 2H), 2.04 (t, J = 2.6 Hz, 1H)), 1.97-1.86 (m, 2H), 1.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.62, 144.49, 110.57, 78.68, 71.41, 56.68, 52.76, 32.07, 30.25, 22.87, 22.42. HRMS-ESI Cald for $C_{13}H_{18}O_4Na$ $[M+Na]^+$: 261.1103. Found: 261.1112.

(*Z*)-Dimethyl 4-(1-methylethenyl)-3-(3,3-bis(methoxycarbonyl)-5-hexenylidene)cyclopentane-1,1-dicarboxylate (140).



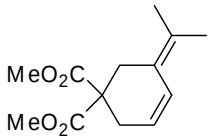
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (ddt, J = 17.2, 9.6, 7.3 Hz, 1H), 5.30 (m, 1H), 5.11 (d, J = 1.7 Hz, 1H), 5.07 (d, J = 2.0 Hz, 1H), 4.76 (m, 2H), 3.75 (s, 3H), 3.72 (s, 6H), 3.71 (s, 3H), 3.33 (t, J = 8.2 Hz, 1H), 2.99, 2.85 (AB system, J_{AB} = 15.6 Hz, 2H), 2.72 (ddd, J = 13.1, 8.8, 1.7 Hz, 1H), 2.68-2.52 (m, 3H), 2.44 (dt, J = 15.5, 4.4 Hz, 1H), 1.99 (dd, J = 13.1, 8.5 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, DEPTQ) δ 171.68 (C), 171.61 (C), 171.41 (C), 171.27 (C), 145.32 (C), 143.24 (C), 132.52 (CH), 119.06 (CH_2), 118.74 (CH), 111.41 (CH_2), 59.00 (C), 57.53 (C), 52.77 (CH_3), 52.68 (CH_3), 52.41 (CH_3), 52.38 (CH_3), 47.13 (CH), 42.96 (CH_2), 39.80 (CH_2), 37.12 (CH_2), 31.45 (CH_2), 19.53 (CH_3). HRMS-ESI Calcd for $C_{22}H_{30}O_8Na^{120}Sn$ $[M+Na]^+$: 445.1838. Found: 445.1834.

Procedure for the silver-catalyzed cyclizations of enynes

The reaction procedure for the cyclizations of enynes **141**, **144**, **144**-d_1, **146** is the same as described below for enyne **148**.

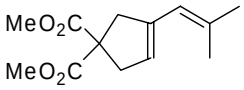
To a solution of **109** (15 mg, 0.02 mmol) in DCE (0.5 mL) was added **148** (50 mg, 0.19 mmol) in DCE (1 mL), the solution was stirred at 23ºC for 4 h then the solvent was removed under reduced pressure and the crude was purified by column chromatography (6:1 hexane-EtOAc) preview deactivation of the silica with triethylamine (5%). This way compounds **149** and **150** are obtained as a mixture 15:1 (47 mg, 94%), for characterization purposes substrates **149** and **150** were separated by column chromatography (100:1 hexane-EtOAc).

Dimethyl 5-Isopropylidene-3-cyclohexene 1,1-dicarboxylate (142).[75]



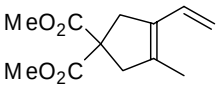
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (dt, *J* = 10.2, 1.7 Hz, 1H), 5.64 (dt, *J* = 10.2, 4.1 Hz, 1H), 3.72 (s, 6H), 2.87 (s, 2H), 2.69 (m, 2H), 1.80 (s, 3H), 1.79 (s, 3H).

Dimethyl-3-(2-methyl-1-propenyl)-3-cyclopentene 1,1-dicarboxylate (143).[76]



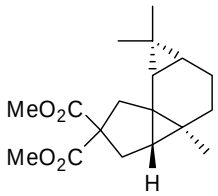
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (s, 1H), 5.39 (s, 1H), 3.71 (s, 6H), 3.20 (d, *J* = 1.4 Hz, 2 H), 3.05 (s, 2H), 1.79 (s, 3H), 1.75 (s, 3H).

Dimethyl-3-ethenyl-4-methyl-3-cyclopentene 1,1-dicarboxylate (145).[68]



^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 16.9, 10.5 Hz, 1H), 5.06 (d, *J* = 11.7 Hz, 1H), 5.01 (d, *J* = 17.8 Hz, 1H), 3.72 (s, 6H), 3.13 (q, *J* = 1.7 Hz, 2H), 3.05 (br s, 2H), 1.77 (s, 3H). The reaction with deuterated enyne **144**-d_1 afforded **145**-d_1 (the signal at 6.54 ppm (1H) disappeared in the ^{1}H NMR).

Tetracycle (147).[62b]

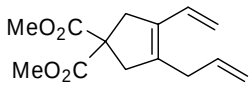


[75] Faller, J. M.; Fontaine, P.P. *J. Organomet. Chem*. **2006**, *691*, 1912-1918.

[76] Hoye, T. R.; Suriano, J. A. *Organometallics* **1992**, *11*, 2044.

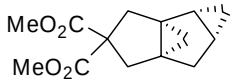
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.67 (s, 3H), 2.54 (dd, *J* = 14.6, 7.3 Hz, 1H), 2.41, 2.77 (AB system, J_{AB} = 14.2 Hz, 2H), 1.97 (dd, *J* = 14.6, 2.6, 1H), 1.78-1.53 (m, 2H), 1.06 (dd, *J* = 7.0, 2.3 Hz, 1H), 1.04-0.75 (m, 3H), 0.92 (s, 3H), 0.88 (s, 3H), 0.64 (td, *J* = 8.4, 6.1 Hz, 1H).

Dimethyl 3-allyl-4-ethenyl-3-cyclopentene-1,1-dicarboxylate (149).



^{1}H NMR (400 MHZ, $CDCl_3$) δ 6.59 (dd, *J* = 17.8, 10.5, 1H), 5.75 (tdd, *J* = 16.7, 10.2, 6.7 Hz, 1H), 5.16-5.01 (m, 4H), 3.76 (s, 6H), 3.20 (s, 2H), 3.09 (s, 2H), 2.96 (d, *J* = 6.4 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 172.56, 136.21, 134.62, 132.14, 129.70, 116.23, 114.55, 56.96, 52.87, 44.33, 40.64, 32.34. HRMS-ESI Calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$: 273.1103. Found: 273.1098.

Tetracycle 150.



^{1}H NMR (400 MHZ, $CDCl_3$) δ 3.72 (s, 3H), 3.70 (s, 3H), 2.56 (d, *J* = 13.8 Hz, 1H), 2.50 (d, *J* = 13.8 Hz, 1H), 2.39 (d, *J* = 13.8 Hz, 1H), 2.12 (d, *J* = 13.8 Hz, 1H), 1.98 (dd, *J* = 12.8, 5.2 Hz, 1H), 1.80 (d, *J* = 12.6 Hz, 1H), 1.40-1.32 (m, 1H), 1.17-1.09 (m, 1H), 0.69-0.61 (m, 2H), 0.59 (d, *J* = 5.5 Hz, 1H), 0.16 (q, *J* = 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.11, 172.28, 66.26, 52.87, 52.72, 44.34, 40.14, 37.83, 37.52, 36.84, 25.88, 24.42, 22.29, 14.53. HRMS-ESI Calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$: 273.1103. Found: 273.115. The structure was confirmed by COSY, HMQC, and NOESY experiments.

Crystal data and structure refinement for complex 109.

Table S-1. Crystal data and structure refinement for **109**.

Empirical formula	$C_{28}H_{39}Ag\ F_6OPSb$
Formula weight	766.18
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	Cc

Unit cell dimensions	a = 10.0619(6) Å = 90°.
	b = 15.9712(9) Å = 102.375(2)°.
	c = 18.7965(11) Å = 90°.
Volume	2950.4(3) $Å^3$
Z	4
Density (calculated)	1.725 Mg/m^3
Absorption coefficient	1.692 mm^{-1}
F(000)	1528
Crystal size	0.30 x 0.30 x 0.20 mm^3
Theta range for data collection	2.78 to 39.50°.
Index ranges	-17<=h<=14, -27<=k<=28, -33<=l<=33
Reflections collected	29910
Independent reflections	13301 [R(int) = 0.0246]
Completeness to theta = 39.50°	92.2 %
Absorption correction	SADABS (Bruker-Nonius)
Max. and min. transmission	0.7284 and 0.6308
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13301 / 2 / 343
Goodness-of-fit on F^2	1.109
Final R indices [I>2sigma(I)]	R1 = 0.0223, wR2 = 0.0601
R indices (all data)	R1 = 0.0227, wR2 = 0.0603
Absolute structure parameter	0.014(8)
Largest diff. peak and hole	1.915 and -0.795 $e.Å^{-3}$

Table 2. Bond lengths [Å] and angles [°] for **132**.

Ag(1)-O(1)	2.1445(10)	C(2)-C(3)	1.3928(18)
Ag(1)-P(3)	2.3405(3)	P(3)-C(19)	1.8389(12)
F(1)-Sb(2)	1.8798(14)	P(3)-C(13)	1.8442(14)
C(1)-C(2)	1.4023(16)	C(3)-C(4)	1.389(2)
C(1)-C(6)	1.4125(17)	C(4)-C(5)	1.394(2)
C(1)-P(3)	1.8250(11)	C(5)-C(6)	1.4057(18)
O(1)-C(28)	1.4464(19)	C(6)-C(7)	1.4897(17)
O(1)-C(25)	1.447(2)	C(7)-C(12)	1.397(2)
Sb(2)-F(3)	1.8722(11)	C(7)-C(8)	1.402(2)
Sb(2)-F(4)	1.8728(13)	C(8)-C(9)	1.398(2)
Sb(2)-F(6)	1.8755(12)	C(9)-C(10)	1.386(3)
Sb(2)-F(2)	1.8778(12)	C(10)-C(11)	1.401(3)
Sb(2)-F(5)	1.8836(12)	C(11)-C(12)	1.392(2)

C(13)-C(14)	1.5352(18)	C(1)-P(3)-C(19)	103.87(5)
C(13)-C(18)	1.5381(17)	C(1)-P(3)-C(13)	109.70(6)
C(14)-C(15)	1.529(2)	C(19)-P(3)-C(13)	105.65(6)
C(15)-C(16)	1.536(2)	C(1)-P(3)-Ag(1)	115.08(4)
C(16)-C(17)	1.529(2)	C(19)-P(3)-Ag(1)	113.66(4)
C(17)-C(18)	1.530(2)	C(13)-P(3)-Ag(1)	108.43(4)
C(19)-C(24)	1.532(2)	C(4)-C(3)-C(2)	119.43(12)
C(19)-C(20)	1.5334(17)	C(3)-C(4)-C(5)	119.96(12)
C(20)-C(21)	1.5293(19)	C(4)-C(5)-C(6)	121.24(13)
C(21)-C(22)	1.523(3)	C(5)-C(6)-C(1)	118.76(11)
C(22)-C(23)	1.531(2)	C(5)-C(6)-C(7)	117.00(11)
C(23)-C(24)	1.539(2)	C(1)-C(6)-C(7)	124.24(10)
C(25)-C(26)	1.501(2)	C(12)-C(7)-C(8)	118.73(13)
C(26)-C(27)	1.508(3)	C(12)-C(7)-C(6)	120.15(13)
C(27)-C(28)	1.527(3)	C(8)-C(7)-C(6)	121.00(13)
O(1)-Ag(1)-P(3)	174.50(4)	C(9)-C(8)-C(7)	120.40(16)
C(2)-C(1)-C(6)	119.03(11)	C(10)-C(9)-C(8)	120.20(17)
C(2)-C(1)-P(3)	118.36(9)	C(9)-C(10)-C(11)	120.03(14)
C(6)-C(1)-P(3)	122.04(8)	C(12)-C(11)-C(10)	119.54(17)
C(28)-O(1)-C(25)	110.71(11)	C(11)-C(12)-C(7)	121.10(17)
C(28)-O(1)-Ag(1)	125.29(10)	C(14)-C(13)-C(18)	110.38(11)
C(25)-O(1)-Ag(1)	124.00(9)	C(14)-C(13)-P(3)	111.35(9)
F(3)-Sb(2)-F(4)	89.91(7)	C(18)-C(13)-P(3)	116.37(9)
F(3)-Sb(2)-F(6)	178.97(8)	C(15)-C(14)-C(13)	110.67(11)
F(4)-Sb(2)-F(6)	91.09(8)	C(14)-C(15)-C(16)	111.64(14)
F(3)-Sb(2)-F(2)	89.97(6)	C(17)-C(16)-C(15)	110.40(13)
F(4)-Sb(2)-F(2)	90.71(7)	C(16)-C(17)-C(18)	111.54(12)
F(6)-Sb(2)-F(2)	89.76(7)	C(17)-C(18)-C(13)	110.59(11)
F(3)-Sb(2)-F(1)	89.87(7)	C(24)-C(19)-C(20)	110.73(11)
F(4)-Sb(2)-F(1)	178.93(8)	C(24)-C(19)-P(3)	111.14(9)
F(6)-Sb(2)-F(1)	89.14(8)	C(20)-C(19)-P(3)	108.91(8)
F(2)-Sb(2)-F(1)	90.34(7)	C(21)-C(20)-C(19)	111.08(11)
F(3)-Sb(2)-F(5)	89.98(6)	C(22)-C(21)-C(20)	111.08(13)
F(4)-Sb(2)-F(5)	88.90(6)	C(21)-C(22)-C(23)	111.01(13)
F(6)-Sb(2)-F(5)	90.29(6)	C(22)-C(23)-C(24)	111.12(13)
F(2)-Sb(2)-F(5)	179.61(7)	C(19)-C(24)-C(23)	110.62(12)
F(1)-Sb(2)-F(5)	90.05(7)	O(1)-C(25)-C(26)	105.39(14)
C(3)-C(2)-C(1)	121.54(12)	C(25)-C(26)-C(27)	102.17(14)

C(26)-C(27)-C(28)	103.58(15)	O(1)-C(28)-C(27)	103.93(15)

Table 3. Torsion angles [°] for S585_0m.

P(3)-Ag(1)-O(1)-C(28)	11.0(5)
P(3)-Ag(1)-O(1)-C(25)	-169.6(3)
C(6)-C(1)-C(2)-C(3)	-0.6(2)
P(3)-C(1)-C(2)-C(3)	170.85(12)
C(2)-C(1)-P(3)-C(19)	-42.11(13)
C(6)-C(1)-P(3)-C(19)	129.10(12)
C(2)-C(1)-P(3)-C(13)	70.44(12)
C(6)-C(1)-P(3)-C(13)	-118.35(12)
C(2)-C(1)-P(3)-Ag(1)	-166.99(10)
C(6)-C(1)-P(3)-Ag(1)	4.22(13)
O(1)-Ag(1)-P(3)-C(1)	-115.0(4)
O(1)-Ag(1)-P(3)-C(19)	125.4(4)
O(1)-Ag(1)-P(3)-C(13)	8.2(4)
C(1)-C(2)-C(3)-C(4)	-1.1(2)
C(2)-C(3)-C(4)-C(5)	1.3(2)
C(3)-C(4)-C(5)-C(6)	0.3(3)
C(4)-C(5)-C(6)-C(1)	-2.1(2)
C(4)-C(5)-C(6)-C(7)	178.06(15)
C(2)-C(1)-C(6)-C(5)	2.2(2)
P(3)-C(1)-C(6)-C(5)	-168.96(11)
C(2)-C(1)-C(6)-C(7)	-177.93(13)
P(3)-C(1)-C(6)-C(7)	10.9(2)
C(5)-C(6)-C(7)-C(12)	68.61(17)
C(1)-C(6)-C(7)-C(12)	-111.28(16)
C(5)-C(6)-C(7)-C(8)	-107.37(16)
C(1)-C(6)-C(7)-C(8)	72.75(18)
C(12)-C(7)-C(8)-C(9)	-0.4(2)
C(6)-C(7)-C(8)-C(9)	175.58(12)
C(7)-C(8)-C(9)-C(10)	0.7(2)
C(8)-C(9)-C(10)-C(11)	-0.2(2)
C(9)-C(10)-C(11)-C(12)	-0.6(2)
C(10)-C(11)-C(12)-C(7)	0.9(2)
C(8)-C(7)-C(12)-C(11)	-0.3(2)
C(6)-C(7)-C(12)-C(11)	-176.39(13)

C(1)-P(3)-C(13)-C(14)	72.29(9)
C(19)-P(3)-C(13)-C(14)	-176.32(8)
Ag(1)-P(3)-C(13)-C(14)	-54.14(9)
C(1)-P(3)-C(13)-C(18)	-55.38(10)
C(19)-P(3)-C(13)-C(18)	56.02(10)
Ag(1)-P(3)-C(13)-C(18)	178.20(8)
C(18)-C(13)-C(14)-C(15)	-56.83(15)
P(3)-C(13)-C(14)-C(15)	172.33(10)
C(13)-C(14)-C(15)-C(16)	56.43(17)
C(14)-C(15)-C(16)-C(17)	-55.48(18)
C(15)-C(16)-C(17)-C(18)	55.68(17)
C(16)-C(17)-C(18)-C(13)	-56.91(15)
C(14)-C(13)-C(18)-C(17)	57.04(14)
P(3)-C(13)-C(18)-C(17)	-174.82(9)
C(1)-P(3)-C(19)-C(24)	-59.97(10)
C(13)-P(3)-C(19)-C(24)	-175.43(8)
Ag(1)-P(3)-C(19)-C(24)	65.81(9)
C(1)-P(3)-C(19)-C(20)	177.77(10)
C(13)-P(3)-C(19)-C(20)	62.32(11)
Ag(1)-P(3)-C(19)-C(20)	-56.44(11)
C(24)-C(19)-C(20)-C(21)	56.49(16)
P(3)-C(19)-C(20)-C(21)	178.98(11)
C(19)-C(20)-C(21)-C(22)	-56.41(17)
C(20)-C(21)-C(22)-C(23)	56.09(16)
C(21)-C(22)-C(23)-C(24)	-56.04(18)
C(20)-C(19)-C(24)-C(23)	-56.15(15)
P(3)-C(19)-C(24)-C(23)	-177.35(10)
C(22)-C(23)-C(24)-C(19)	56.09(18)
C(28)-O(1)-C(25)-C(26)	-14.20(18)
Ag(1)-O(1)-C(25)-C(26)	166.31(11)
O(1)-C(25)-C(26)-C(27)	32.03(19)
C(25)-C(26)-C(27)-C(28)	-37.6(2)
C(25)-O(1)-C(28)-C(27)	-9.56(19)
Ag(1)-O(1)-C(28)-C(27)	169.92(13)
C(26)-C(27)-C(28)-O(1)	29.4(2)